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(54) Title: DETERMINING CANCER-LINKED GENES AND THERAPEUTIC TARGETS USING MOLECULAR CYTOGENETIC METHODS

(57) Abstract: Methods for identifying potential therapeutic agents, such as anti-tumor agents, based on their modulation of the expression of specified genes, especially genes mapping to specific chromosomal regions, are disclosed. Also described are methods for diagnosing cancerous, or potentially cancerous, conditions as a result of the expression, or patterns of expression, of such genes, including detecting changes in levels of gene copy number and/or level of amplification of the said gene, or sets of genes, to detect and/or diagnose the cancer. Methods for detecting or determining functionally related genes, as well as methods for treating cancer based on targeting expression products of such genes, determining genes involved in the cancerous process and the success and/or response rates and survival statistics for cancer patients on treatment are encompassed by the invention. Also encompassed are methods involving determining the modulated expression of the genes in these regions of interest (ROIs) as pharmacodynamic/pharmacogenetic/surrogate markers and/or for patient profiling prior to accrual for clinical trials/treatments based on the identification of these genes as validated gene/drug targets in various cancer tissue types.

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# **DETERMINING CANCER-LINKED GENES AND THERAPEUTIC TARGETS USING MOLECULAR CYTOGENETIC METHODS**

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10           This application claims priority of U.S. Provisional Application Serial  
No. 60/462,895, filed 15 April 2003, the disclosure of which is hereby  
incorporated by reference in its entirety.

15

## **FIELD OF THE INVENTION**

20           The present invention relates to identification of genes whose  
disruption and/or change in expression is useful to distinguish cancerous from  
non-cancerous tissue and serve as potential therapeutic targets,  
pharmacodynamic /pharmacogenetic/surrogate and prognostic and diagnostic  
25   Genomic Hybridization (CGH) and Spectral Karyotyping (SKY)/fluorescent *in*  
*situ* hybridization (FISH) analysis of DNA and chromosomes of various cancer  
cell lines and primary and metastatic tumor samples combined with gene  
expression analysis of these cells and tissues.

30

## **BACKGROUND OF THE INVENTION**

Chromosomal abnormalities have been identified in most cancer cells.  
Conventional chromosome banding techniques allow for the detection of  
35   specific chromosomal defects in tumor cells but interpretation of the banding  
pattern is sometimes difficult, particularly when complex chromosomal

rearrangements or subtle abnormalities are present. In recent years, new techniques, such as CGH and SKY, based on fluorescent *in situ* hybridization (FISH) (Pinkel et al., Proc Nat Acad Sci USA 85:9138-42 (1988)) have been developed to overcome the limitations of conventional chromosome banding.

5 CGH measures intensities of fluorescently labeled tumor DNA and normal DNA following hybridization to normal chromosomes (Kallioniemi et al., Science 258:818-21 (1992)). Gain or loss of copy number of a particular chromosome or chromosome region in the tumor DNA is determined by the relative intensity of a fluorescence ratio. SKY utilizes a cocktail of

10 chromosome probes, fluorescently labeled to specify each chromosome, which is hybridized to tumor chromosomes in an effort to identify numerical and structural abnormalities in the tumor cell (Schröck et al., Science 273:494-7 (1996)). CGH and SKY have been used to identify chromosomal regions that harbor genes significant to the process of tumor initiation or

15 progression.

#### BRIEF SUMMARY OF THE INVENTION

20 In one aspect the present invention relates to a set of genes that have been localized within human chromosomal regions of interest (ROI) that have been identified by molecular cytogenetic techniques.

In one aspect, the present invention relates to a method for diagnosing

25 cancer in a mammal, especially a human patient, comprising determining amplification of a gene in the genome of a mammal wherein said gene is a gene of Table 1.

In a preferred embodiment thereof, the cancer is a member selected

30 from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

In another preferred embodiment thereof, 3. The method of claim 1 wherein said gene of Table 1 is a gene that encodes the same gene product as a polynucleotide selected from the polynucleotides of SEQ ID NO: 1 – 805 and 855 - 923.

5

In another embodiment, the present invention relates to a method for diagnosing cancer or a pre-cancerous condition in a mammal, comprising:

(a) obtaining a cell or tissue sample from a mammal, especially a human patient, suspected of having cancer or a pre-cancerous condition and  
10 determining for said sample the gene copy number of a gene of Table 1;

(b) comparing said gene copy number of step (a) to the gene copy number of the same gene from a sample of a corresponding cell or tissue from a mammal of the same species not having cancer of the type being diagnosed

15 whereby a higher gene copy number determined in step (a) relative to that in step (b) indicates the presence of a cancer or pre-cancerous condition in the mammal of step (a) and results in a diagnosis of cancer or a pre-cancerous condition in said mammal.

20 In a preferred embodiment of the methods of the invention, said molecule is a member selected from an antisense DNA, an antisense RNA, a ribozyme and an siRNA.

In another embodiment, the present invention relates to a method for  
25 identifying an agent having therapeutic activity in a human patient in need of said therapeutic activity, comprising:

(a) determining in a sample from a patient the level of a gene product encoded by a gene of Table 1 prior to administering a test compound to said patient;

30 (b) administering said test compound to said patient;

(c) determining in a sample from said patient the level of a gene product encoded by the same the gene as in step (a)



wherein a decrease in the level of said gene product in step (c) relative to step (a) identifies said test compound as an agent having therapeutic activity.

5 In a further embodiment, the present invention relates to a method for identifying an antineoplastic agent, comprising:

(a) contacting a test compound with a cell that expresses a gene of Table 1; and

10 (b) determining a change in gene expression as a result of said contacting;

whereby said change in said gene expression identifies said test compound as an antineoplastic agent.

15 The present invention also relates to a method for determining the cancerous status of a cell, comprising determining elevated expression in said cell of a gene of Table 1 wherein elevated expression of said gene indicates that said cell is cancerous.

20 In an additional embodiment, the present invention relates to a method for identifying a compound as an anti-neoplastic agent, comprising:

(a) contacting a test compound with a polypeptide encoded by a gene of Table 1,

(b) determining a change in a biological activity of said polypeptide due to said contacting,

25 wherein a change in activity identifies said test compound as an agent having antineoplastic activity.

30 In a preferred embodiment of the foregoing, the polypeptide is an enzyme selected from kinase, protease, peptidase, phosphodiesterase, phosphatase, dehydrogenase, reductase, carboxylase, transferase, deacetylase and polymerase.

The present invention also relates to a method for identifying an anti-neoplastic agent comprising contacting a cancerous cell with a compound found to have anti-neoplastic activity in other the methods of the invention under conditions promoting the growth of said cell and detecting a change in  
5 the activity of said cancerous cell.

The present invention further relates to a method for treating cancer comprising contacting a cancerous cell with an agent having affinity for an expression product of a gene of Table 1 and in an amount effective to cause a  
10 reduction in cancerous activity of said cell.

The present invention also contemplates a method for monitoring the progress of cancer therapy in a patient comprising monitoring in a patient undergoing cancer therapy the expression of a gene of Table 1.  
15

In addition, the present invention encompasses a method for determining the likelihood of success of cancer therapy in a patient, comprising monitoring in a patient undergoing cancer therapy the expression of a gene of Table 1 wherein a decrease in said expression prior to  
20 completion of said cancer therapy is indicative of a likelihood of success of said cancer therapy.

In another embodiment, the present invention relates to a method for producing test data with respect to the anti-neoplastic activity of a compound  
25 comprising:

- (a) identifying a test compound as having anti-neoplastic activity using other methods of the invention;
- (b) producing test data with respect to the anti-neoplastic activity of said test compound sufficient to identify the chemical structure of said test  
30 compound.

Additionally, the present invention encompasses a method for determining the progress of a treatment for cancer in a patient afflicted therewith, following commencement of a cancer treatment on said patient, comprising:

(a) determining in said patient a change in expression of one or more  
5 genes of Table 1; and

(b) determining a change in expression of said gene compared to expression of said one or more determined genes prior to said cancer treatment;

wherein said change in expression indicates progress of said treatment  
10 thereby determining the progress of said treatment.

#### **SEQUENCE LISTING ON CD-ROM ONLY**

15

The sequences disclosed herein as SEQ ID NO: 1-923 in the sequence listing are contained on compact disc (CD-ROM) only, which accompanies this application and the contents of said CD-ROMs are hereby incorporated by reference in their entirety. These sequence numbers also appear in Table  
20 1 where all sequences are referred to as consecutive serial numbers for reference purposes only.

25

#### **DETAILED SUMMARY OF THE INVENTION**

The present invention relates to a set of genes that are amplified and/or over-expressed genes in cancer cell lines and have been localized to various chromosomal regions of interest. These genes have been identified  
30 through a combination of CGH, SKY, expression analysis and Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR). Such genes are both markers and potential therapeutic targets for cancer, in particular breast,

colon, lung and prostate malignancies. In addition, the amplified nature of such genes provides a means of diagnosing a cancerous condition, or predisposition to a cancerous conditions, by determining the amplification of one or more of such genes in a patient afflicted with, or predisposed toward,  
5 or otherwise at risk of developing, cancer.

In accordance with the present invention, a number of genes have been localized to a chromosomal regions of interest as identified in Table 1 (serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805  
10 (prostate), serial number 806-923 (transcript or protein)). The invention also includes any subsets of these. As described herein, these sequences include DNA sequences of SEQ ID NO: 1 – 805, transcripts with the sequences of SEQ ID NO: 855 – 923, and proteins/polypeptides with amino acid sequences of SEQ ID NO: 806 - 854.

15

Briefly, the procedures used to identify the genes disclosed herein may be summarized as follows:

For CGH analysis, based on detailed molecular cytogenetic  
20 characterizations, the following data sets are generated, which may include regions reported in the public domain as well as unique regions not previously known.

- 25 1. A map of chromosomal regions involved in consistent, recurrent and high level genomic gains (i.e., amplifications) for a representative cancer cell line or tumor type (e.g. colon, prostate, breast and lung) that can be recognized as a pattern/signature for a given tumor type.
2. A map of chromosomal regions containing genomic losses (i.e., deletions) in each tumor type and individual cell line to be examined.
- 30 3. Levels of intensities of gains and losses categorized for entry into a database.

4. A comparison of the patterns of gains and losses between the clinical samples (e.g. colon xenografts) and cell lines (e.g., colon) of matched Stages and Grades.
5. A comparison of the patterns of gains and losses between primary prostate tumor cell lines (e.g., CPDR lines) and metastatic prostate tumor cell lines (e.g., DU 145, PC3 and LNCaP).

In accordance with the present invention, for SKY analysis, data sets were generated according to the following steps:

- 10 1. Identification and development of a database of novel chromosomal rearrangements in epithelial cancer cell lines.
2. Identification of novel translocations involving specific chromosomes or chromosomal regions
- 15 3. Reconciliation of SKY and CGH analysis on the same cell line as a verification of the combined findings.

Combining genomic DNA analysis of gains and losses in the tumor cell lines/clinical samples with cDNA expression analysis from matched tumor types displayed on a genome template from the Golden Path genome browser using a Spotfire™ analysis tool:

- 25 1. A pattern of gene expression on a U-95 Affymatix chip set obtained via the Gene Logic database was used to generate differential gene expression profiles between samples sets containing normal and malignant tissues from colon, prostate, lung, breast and various cell lines.
2. A Spotfire™ visualization tool was developed that allowed the generation of a list of all the genes that are present in the Golden Path within the clustered regions of gains/losses for each cell type/tumor type to generate the gene sets to include in the HITS platform
- 30 3. The following algorithm was employed:

- 5
- i) Match chromosomal regions of amplification/gains defined by CGH with the location of genes/ESTs on an Affymatrix chip as mapped to a Golden Path genome template.
  - ii) Identify genes/ESTs over-expressed in tumor tissue compared to normal tissue in said chromosomal regions using the Gene Logic database.
  - iii) Compile data on cell lines of a particular tumor type and different tumor types showing clusters of genomic gains and losses at certain chromosomal regions.
  - 10 iv) Pick BACs that span the chromosomal regions consistently gained and containing over-expressed genes in an effort to positionally clone novel cancer genes (oncogenes and genes in relevant pathways)
  - v) Validate the identified genes by
  - 15 A) Picking STS markers that identify the gene sequence and quantify the relative copy number in genomic DNA and RNA across a panel of tumor cell lines.
  - B) Develop probes for FISH on chromosomes from tumor cell lines and primary tumor tissue micro-arrays.

20

4. The expression data from tumor cell lines that have undergone SKY/CGH analysis was used to pick candidate genes to validate as individual targets in functional genomic assays and in-vivo assays and for use in the transcriptional assay platform.

25

In accordance with the present invention, over-expression of cellular genes is conveniently monitored in model cellular systems using cell lines (such as is used in the example below), primary cells, or tissue samples maintained in growth media. For different purposes, these may be treated with compounds at one or more different concentrations to assay for modulating agents. Thus, cellular RNAs were isolated from the cells or cultures as an indicator of selected gene expression. The cellular RNAs were then divided

30

and subjected to analysis that detected the presence and/or quantity of specific RNA transcripts, which transcripts were then amplified for detection purposes using standard methodologies, such as reverse transcriptase polymerase chain reaction (RT-PCR). The levels of specific RNA transcripts, including their presence or absence, were determined. When used for identification of modulating agents, such as anti-neoplastic agents, a metric is derived for the type and degree of response of the treated sample compared to control samples.

10 In accordance with the foregoing, the genes identified as being amplified and/or over-expressed, which can include increased copy number thereof, in cancerous cells are localized in chromosomal regions of interest as identified in Table 1 (serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate); for polypeptide SEQ ID NOs, see Table 1, 15 serial number 806-923 (transcript or protein)).

These genes may be utilized to characterize, the cancerous, or non-cancerous, status of cells, or tissues. The methods of the invention may be used with a variety of cell lines or with primary samples from tumors maintained *in vitro* under suitable culture conditions for varying periods of time, or *in situ* in suitable animal models.

25 The genes disclosed herein are expressed at levels in cancer cells that are different from the expression levels in non-cancer cells. These genes as identified in Table 1 are amplified in cancer cells relative to non-cancer cells of corresponding tissues, especially breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

30

In accordance with the foregoing, the present invention relates to a method for diagnosing cancer in a mammal, comprising determining amplification of a gene in the genome of a mammal wherein said gene is a gene of Table 1.

5

In a preferred embodiment thereof, said gene of Table 1 is a gene that encodes the same gene product as a polynucleotide selected from the polynucleotides of SEQ ID NO: 1 – 805 and 855 - 923. In a further preferred embodiment, said mammal is a human patient.

10

The present invention is also directed to a method for diagnosing cancer or a pre-cancerous condition in a mammal, preferably a human patient, comprising:

(a) obtaining a cell or tissue sample from a mammal suspected of having cancer or a pre-cancerous condition and determining for said sample the gene copy number of a gene of Table 1;

(b) comparing said gene copy number of step (a) to the gene copy number of the same gene from a sample of a corresponding cell or tissue from a mammal of the same species not having cancer of the type being diagnosed

20

whereby a higher gene copy number determined in step (a) relative to that in step (b) indicates the presence of a cancer or pre-cancerous condition in the mammal of step (a) and results in a diagnosis of cancer or a pre-cancerous condition in said mammal.

25

In specific embodiments, the cancer to be diagnosed is one or more of breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

Preferably, the gene of Table 1 is a gene that encodes the same gene product as a polynucleotide of SEQ ID NO: 1 – 805 and 855– 923.

30



The present invention is also directed to a method of inhibiting cancer, or a pre-cancerous condition, in a mammalian cell, comprising contacting said cell with a molecule that inhibits function of a gene of Table 1. Preferably, the gene of Table 1 is a gene that encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923. In a specific embodiment thereof, said molecule inhibits gene function by binding to said gene. In other embodiments, the molecule inhibits gene function by binding to an RNA encoded by said gene or inhibits gene function by binding to polypeptide encoded by said gene. Preferably, the molecule is a member selected from an antisense DNA, an antisense RNA, a ribozyme and an siRNA. Also preferred is where the cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

The invention contemplates that such contacting occurs in vivo.

The invention also relates to a method for identifying an agent having therapeutic activity in a human patient in need of said therapeutic activity, comprising:

(a) determining in a sample from a patient the level of a gene product encoded by a gene of Table 1 prior to administering a test compound to said patient;

(b) administering said test compound to said patient;

(c) determining in a sample from said patient the level of a gene product encoded by the same the gene as in step (a)

wherein a decrease in the level of said gene product in step (c) relative to step (a) identifies said test compound as an agent having therapeutic activity.

Preferably, said therapeutic activity is anticancer activity and said cancer is one or more of breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

Also preferred is where said gene product is an RNA or a polypeptide, especially where an activity of the polypeptide is determined, preferably an enzyme activity. In specific embodiments, said gene of Table 1 is a gene that encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805  
5 and 855 - 923, as well as where said molecule is a member selected from an antisense DNA, an antisense RNA, a ribozyme and an siRNA.

The present invention also relates to a method for identifying an antineoplastic agent, comprising:

10 (a) contacting a test compound with a cell that expresses a gene of Table 1; and

(b) determining a change in gene expression as a result of said contacting;

whereby said change in said gene expression identifies said test  
15 compound as an antineoplastic agent.

Most preferred is where the change in expression is a decrease in expression. The contacting may occur *in vivo*. Also preferred is where said gene of Table 1 encodes the same gene product as a polynucleotide of  
20 SEQ ID NO: 1 - 805 and 855 - 923 and where said molecule is a member selected from an antisense DNA, an antisense RNA, ribozyme, an siRNA, a small organic molecule and an antibody.

The present invention also relates to a method for determining the  
25 cancerous status of a cell, comprising determining elevated expression in said cell of a gene of Table 1 wherein elevated expression of said gene indicates that said cell is cancerous. Preferably, wherein said elevated expression is an elevated copy number of the gene and wherein said gene of Table 1 encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 -  
30 923.

The present invention further relates to a method for identifying a compound as an anti-neoplastic agent, comprising:

(a) contacting a test compound with a polypeptide encoded by a gene of Table 1,

5 (b) determining a change in a biological activity of said polypeptide due to said contacting,

wherein a change in activity identifies said test compound as an agent having antineoplastic activity.

10 Preferably, said gene of Table encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923.

In a preferred embodiment, the change in biological activity is a decrease in biological activity.

15

In another preferred embodiment, the biological activity is an enzyme activity, such as where the enzyme is one selected from the group kinase, protease, peptidase, phosphodiesterase, phosphatase, dehydrogenase, reductase, carboxylase, transferase, deacetylase and polymerase.

20

Assays for these enzymes are available, such as for phosphodiesterases (the most pharmacologically relevant phosphodiesterases are those that hydrolyze cyclic nucleotides (see, for example, cAMP and cGMP assays available from Perkin-Elmer, as well as  
25 Estrade et al., Eur. J. Pharmacol. 352:2-3, 157-163 (1998)).

Protein phosphatases remove phosphate residues from proteins. Most tests of their activity use the same assays as for protein kinases. A non-radioactive phosphatase assay system is available from Promega  
30 Biotech.

The therapeutically most relevant dehydrogenases oxidize or reduce small molecular weight metabolites, esp. steroid hormones, or that generally use or generate NAD or NADP (see: Haeseleer et al., J. Biol. Chem., 273:21790-21799 (1998)). A commercial assay is available from  
5 Cayman Chemical (at [www.caymanchem.com](http://www.caymanchem.com)).

Gamma-carboxylases are important enzymes in the blood coagulation process. The main assay protocols use synthetic peptides (see: Ulrich et al., J. Biol. Chem., 263:9697-9702 (1988); Begley et al.,  
10 J. Biol. Chem., 275:36245-36249 (2000)).

In highly preferred embodiments, the kinase is one of a protein kinase, a serine or threonine kinase, or a receptor tyrosine protein kinase. Where the  
15 polypeptide encoded by a gene of the invention is a protein kinase, especially involving tyrosine kinase, various assays for activity are available. Protein kinases add phosphate groups to serine, threonine or tyrosine residues on proteins, most commonly measured with phospho-serine, threonine, or tyrosine-specific antibodies, or generation of radiolabeled substrate, or  
20 consumption of ATP, or phosphorylation of (synthetic) small peptides, or measuring downstream enzyme activity and gene transcription. Such assays are commercially available. (See, for example, the tyrosine kinase assay from Roche Molecular Biochemicals). Assays for serine/threonine kinases are also available at Chromagen.com, Upstate Biotechnology,  
25 Inc. (Lake Placid, NY, and at [upstatebiotech.com](http://upstatebiotech.com)) and from Applied BioSystems (Foster City, CA ([home.appliedbiosystems.com](http://home.appliedbiosystems.com))).

In other specific embodiments, the protease is a serine protease, cysteine protease or aspartic acid protease, or the transferase is a  
30 methyltransferase, preferably a cytosine methyltransferase or an adenine methyltransferase, or the deacetylase is a histone deacetylase, or the

carboxylase is a  $\gamma$ -carboxylase, or the peptidase is a zinc peptidase, or the polymerase is a DNA polymerase or an RNA polymerase.

Proteases degrade proteins, un-specifically or at specific sites.

5 Almost all pharmacologically relevant ones have very narrowly defined specific substrates, and their activity is most often measured by directly measuring cleavage product or generation of (fluorescent) light after cleavage of synthetic substrates. Assays are available for serine proteases (Calbiochem, Palo Alto, CA, and see Berdichevsky et al., J. Virol. Methods, 107:245-255 (2003), for cysteine proteases (See: Schulz et al., Mol. Pathol., 51:222-24 (1998) and Selzer et al., PNAS, 96:11015-11022 (1999)), for aspartic acid proteases (Geno Tech, Inc. at [www.genotech.com](http://www.genotech.com)) and for zinc peptidases (see Evans et al., J. Biol. Chem., 278:23180-23186 (2003)).

15

Both (regulatory) DNA-methylases and (biosynthetic) protein methylases that are drug targets. (See: Jonassen and Clarke, J. Biol. Chem., 275:12381-12387 (2000); Jackson et al., Nature, 416:556-560 (2002)).

20

Most HDAC (histone deacetylase) assays use colorimetric or fluorometric (synthetic) substrates. Standard assays are for binding, especially molecular size changes, blocking a specific site, and effects on transcription or downstream reactions (if DNA or RNA is the direct target of a drug). A commercial assay is available from Vinci Biochem (at [www.vincibiochem.it](http://www.vincibiochem.it)).

25 In another specific embodiment, the biological activity is a membrane transport activity, preferably wherein the polypeptide is a cation channel protein, an anion channel protein, a gated-ion channel protein or an ABC

transporter protein. Drug effects on the activity of transporter and channel proteins are screened by measuring increase or decrease of the ((radio-)labeled) transported entity inside or outside the cell, in cell-based assays, ATP consumption (in the case of ATPases), or changes in cell membrane potential. Assays employing such proteins are available, such as for ABC transporter (see: Marcil et al., *Lancet*, 354:1341-46 (1999) and for ion channels (from Evotec OAI, at [www.evotecoai.com](http://www.evotecoai.com) and from PharmaLinks, at [www.pharmalinks.org/research/cellsignalling](http://www.pharmalinks.org/research/cellsignalling)).

10 In one embodiment, the polypeptide is an integrin (the signal transduction pathways elicited by the integrins are slow and not very well characterized, hence most assays are either just binding assays or measure downstream biological phenomena (such as migration, invasion, etc.) (See: Ganta et al., *Endocrinology*, 138:3606-3612 (1997); Sim et al., *J. Biomed. Mater. Research*, 68A:352-359 (2004); and Weinreb et al., *Anal. Biochem.*, 306:305-313 (2002)), or a Cytochrome P450 enzyme (almost all cytochrome assays require knowledge of what the substrate is and measure conversion of substrate (free or (radio-)labeled) or generation of product; useful C<sup>14</sup>-labeled substrates are available from Amersham Biosciences at [www1.amershambiosciences.com](http://www1.amershambiosciences.com)), or a nuclear hormone receptor (Assays available from Discoverx, Fremont, CA, such as an estrogen assay; also see Rosen et al., *Curr. Opin. Drug. Discov. Devel.*, 6:224-30 (2003)).

25 In one preferred embodiment, the biological activity is a receptor activity, preferably where the receptor is a G-protein-coupled receptor (GPCR).

GPCRs are transmembrane proteins that wind 7 times back and forth through a cell's plasma membrane with a ligand binding site located on the outside of the membrane surface of the cell and the effector site

being present inside the cell. These receptors bind GDP and GTP. In response to ligand binding, GPCRs activate signal transduction pathways which induce a number of assayable physiological changes, e.g., an increase in intracellular calcium levels, cyclic-AMP, inositol phosphate turnover, and downstream gene transcription (directly or via reporter-assays) along with other translocation assays available for measuring GPCR activation when the polypeptide encoded by a gene of the invention is a GPCR. Thus, such proteins work through a second messenger. The result is activation of CREB, a transcription factor that stimulates the production of gene products. One useful assay is the so-called BRET2/arrestin assay, useful in screening for compounds that interact with GPCRs. (See: Bertrand et al, J. Recept. Signal Transduct Res., 22:533-41 (Feb.-Nov. 2002)). In addition, numerous assays are commercially available, such as the Transfluor Assay, available from Norak Biosciences, Inc. (www.norakbio.com) or ArrayScan and KineticScan, both from Cellomics, or assays from CyBio (Jena, Germany).

Assays useful with the invention are usually set up to screen for agonists or antagonists after adding ligand, but effects on most of these parameters can be measured whether or not the ligand for the receptor is known. Such assays may involve radioligand-binding assays. Activation of the majority of GPCRs by agonists leads to the interaction of beta-arrestin (a protein that is involved in receptor desensitization and sequestration) with the receptor, which is measurable by fluorescence energy transfer

25

The disclosure of all journal articles, or other publications, referred to herein are hereby incorporated by reference in their entirety.

In one embodiment, the polypeptide is in a solution or suspension and contact with the test compound is by direct contact between the test compound and the protein molecule. Alternatively, the polypeptide may be in

30

a cell and the test compound may have to diffuse into the cell in order to contact the polypeptide. In an alternative embodiment, the test compound may be contacted with a cell that contains or expresses the polypeptide but the test compound may have no direct contact with the polypeptide. In stead,  
5 the test compound may act to induce production and/or activity of a different compound, such as an intracellular second messenger that serves to contact the polypeptide and modulate or change the biological activity of this polypeptide.

10 In accordance with the foregoing, the method of the present invention includes cancer modulating agents that are themselves either polypeptides, or small chemical entities, that affect the cancerous process, including initiation, suppression or facilitation of tumor growth, either *in vivo* or *ex vivo*. Such agents may also be antibodies that react with one or more polypeptides  
15 encoded by genes as disclosed herein, preferably polypeptides comprising any one of the amino acid sequences of SEQ ID NO: 806 – 854.

Because the genes disclosed herein are over-expressed and relate to the cancerous condition of a cell, successful anti-neoplastic activity will  
20 commonly be exhibited by agents that reduce the expression of said genes as identified in Table 1. In one embodiment thereof, the change in expression is a decrease in copy number of the gene or genes under study. In accordance therewith, said change in gene copy number is conveniently determined by detecting a change in expression of messenger RNA encoded by said gene  
25 sequence. In another preferred embodiment, expression is determined for more than one such gene, such as 2, 5, 10 or more of the genes.

Other methods useful in measuring a change in expression of the genes disclosed herein include measuring a change in the amount or rate of  
30 synthesis of a polypeptide encoded by said gene, preferably a decrease in synthesis of said polypeptide. Most preferably, the polypeptide comprises an



amino acid sequence highly homologous to a sequence for genes as identified in Table 1 (SEQ ID NO: 1 – 923).

5 The methods of the invention can thus be utilized to identify anti-neoplastic agents useful in treatment of cancerous conditions. Such activity can be further modified by first identifying such an agent using an assay as already described and further contacting such agent with a cancerous cell, followed by monitoring of the status of said cell, or cells. A change in status indicative of successful anti-neoplastic activity may include a decrease in the  
10 rate of replication of the cancerous cell(s), a decrease in the total number of progeny cells that can be produced by said cancerous cell(s), or a decrease in the number of times said cancerous cell(s) can replicate, or the death of said cancerous cell(s).

15 Anti-neoplastic agents may also be identified using recombinant cells suitably engineered to contain and express the cancer-related genes disclosed herein. In one such embodiment, a recombinant cell is formed using standard technology and then utilized in the assays disclosed herein. Methods of forming such recombinant cells are well known in the literature. See, for  
20 example, Sambrook, et al., *Molecular Cloning: A Laboratory Manual*, Second Edition, Cold Spring Harbor, N.Y., (1989), Wu et al, *Methods in Gene Biotechnology* (CRC Press, New York, NY, 1997), and *Recombinant Gene Expression Protocols*, in *Methods in Molecular Biology*, Vol. 62, (Tuan, ed., Humana Press, Totowa, NJ, 1997), the disclosures of which are hereby  
25 incorporated by reference.

The present invention also relates to a method for detecting the cancerous status of a cell, comprising detecting elevated copy number and/or expression in said cell of at least one gene that maps to the chromosomal  
30 region of interest as identified in Table 1 (SEQ ID NO: 1 – 923). Such elevated expression may be readily monitored by comparison to that of otherwise normal cells having the same genes. Elevated expression of these

genes is indicative of the cancerous state. This includes a gene corresponding to a polynucleotide that comprises a nucleotide sequence as identified in Table 1 (SEQ ID NO: 1 – 923). Such elevated expression, including increased copy number, may be the expression of more than one  
5 such gene.

The present invention also relates to a method for detecting a cancer-linked gene comprising the steps of contacting a compound identified as having gene modulating activity for a gene corresponding to a polynucleotide  
10 that comprises a nucleotide sequence as identified in Table 1 (SEQ ID NO: 1 – 923) with a cell expressing a test gene and detecting modulation, such as decreased activity, of such test gene relative to when said compound is not present thereby identifying said test gene as a cancer-related gene. In preferred embodiments, the gene determined by said method is an oncogene,  
15 or cancer facilitating gene.

In another embodiment, there is provided a method for treating cancer comprising contacting a cancerous cell with an agent first identified as having gene modulating activity using any of the assay methods disclosed according  
20 to the invention and in an amount effective to reduce the cancerous activity of said cell. In a preferred embodiment, the cancerous cell is contacted *in vivo*. In other preferred embodiments, said reduction in cancerous activity is a decrease in the rate of proliferation of said cancerous cell, or said reduction in cancerous activity is the death of said cancerous cell.

25 The present invention further relates to a method for treating cancer comprising contacting a cancerous cell with an agent having activity against an expression product encoded by a gene corresponding to a polynucleotide comprising a nucleotide sequence as identified in Table 1 (SEQ ID NO: 1 –  
30 923) where the product is a polypeptide, most preferably one comprising an amino acid sequence as identified in Table 1 (SEQ ID NO: 806 - 854). In a

preferred embodiment, said cancerous cell is contacted *in vivo*. In another preferred embodiment, the agent is an antibody.

As noted, the genes useful in the assay methods include genes  
5 mapping within chromosomal regions of interest and genes as identified in  
Table 1 (SEQ ID NO: 1 – 923), or a gene that encodes the same RNA, such  
as the same messenger RNA, whose corresponding cDNA is one of the  
sequences as identified in Table 1 (SEQ ID NO: 1 – 923). The genes useful in  
the methods of the invention further include genes encoding RNAs whose  
10 corresponding cDNA is at least 90% identical to a sequence as identified in  
Table 1 (SEQ ID NO: 1 – 923), preferably at least about 95% identical to such  
a sequence, more preferably at least about 98% identical to such sequence  
and most preferably one comprising that sequence are specifically  
contemplated by all of the methods of the present invention.

15

In addition, sequences encoding the same proteins (SEQ ID NO: 806 –  
854) as any of these sequences, regardless of the percent identity of such  
sequences, are also specifically contemplated by the invention.

20 The sequences disclosed herein may be genomic in nature and thus  
represent the sequence of an actual gene, such as a human gene, or may be  
a cDNA sequence derived from a messenger RNA (mRNA) and thus  
represent contiguous exonic sequences derived from a corresponding  
genomic sequence or they may be wholly synthetic in origin for purposes of  
25 testing. As described in the Example, the expression of these cancer-related  
genes is determined from the relative expression levels of the RNA  
complement of a cancerous cell relative to a normal (i.e., non-cancerous) cell.  
Because of the processing that may take place in transforming the initial RNA  
transcript into the final mRNA, the sequences disclosed herein may represent  
30 less than the full genomic sequence. They may also represent sequences  
derived from ribosomal and transfer RNAs. Consequently, the genes present  
in the cell (and representing the genomic sequences) and the sequences

disclosed herein, which are mostly cDNA sequences, may be identical or may be such that the cDNAs contain less than the full genomic sequence. Such genes and cDNA sequences are still considered corresponding sequences because they both encode similar RNA sequences. Thus, by way of non-limiting example only, a gene that encodes an RNA transcript, which is then processed into a shorter mRNA, is deemed to encode both such RNAs and therefore encodes an RNA complementary to (using the usual Watson-Crick complementarity rules), or that would otherwise be encoded by, a cDNA (for example, a sequence as disclosed herein). Thus, the sequences disclosed herein correspond to genes contained in the cancerous or normal cells used to determine relative levels of expression because they represent the same sequences or are complementary to RNAs encoded by these genes. Such genes also include different alleles and splice variants that may occur in the cells used in the methods of the invention.

The genes of the invention "correspond to" a polynucleotide having a sequence as identified in Table 1 (SEQ ID NO: 1 – 923) if the gene encodes an RNA (processed or unprocessed, including naturally occurring splice variants and alleles) that is at least 90% identical, preferably at least 95% identical, most preferably at least 98% identical to, and especially identical to, an RNA that would be encoded by, or be complementary to, such as by hybridization with, a polynucleotide having the indicated sequence. In addition, genes including sequences at least 90% identical to a sequence as identified in Table 1 (SEQ ID NO: 1 – 923), preferably at least about 95% identical to such a sequence, more preferably at least about 98% identical to such sequence and most preferably comprising such sequence are specifically contemplated by all of the methods of the present invention as being genes that correspond to these sequences. In addition, sequences encoding the same proteins as any of these sequences, regardless of the percent identity of such sequences, are also specifically contemplated by any of the methods of the present invention that rely on any or all of said sequences, regardless of how they are otherwise described or limited. Thus,

any such sequences are available for use in carrying out any of the methods disclosed according to the invention. Such sequences also include any open reading frames, as defined herein, present within any of the sequences as identified in Table 1 (SEQ ID NO: 1 – 805 and 855 - 923).

5

Further in accordance with the present invention, the term "percent identity" or "percent identical," when referring to a sequence, means that a sequence is compared to a claimed or described sequence after alignment of the sequence to be compared (the "Compared Sequence") with the described or claimed sequence (the "Reference Sequence"). The Percent Identity is then determined according to the following formula:

$$\text{Percent Identity} = 100 [1-(C/R)]$$

wherein C is the number of differences between the Reference Sequence and the Compared Sequence over the length of alignment between the Reference Sequence and the Compared Sequence wherein (i) each base or amino acid in the Reference Sequence that does not have a corresponding aligned base or amino acid in the Compared Sequence and (ii) each gap in the Reference Sequence and (iii) each aligned base or amino acid in the Reference Sequence that is different from an aligned base or amino acid in the Compared Sequence, constitutes a difference; and R is the number of bases or amino acids in the Reference Sequence over the length of the alignment with the Compared Sequence with any gap created in the Reference Sequence also being counted as a base or amino acid.

If an alignment exists between the Compared Sequence and the Reference Sequence for which the percent identity as calculated above is about equal to or greater than a specified minimum Percent Identity then the Compared Sequence has the specified minimum percent identity to the Reference Sequence even though alignments may exist in which the

hereinabove calculated Percent Identity is less than the specified Percent Identity.

As used herein, the terms "portion," "segment," and "fragment," when used in relation to polypeptides, refer to a continuous sequence of residues, such as amino acid residues, which sequence forms a subset of a larger sequence. For example, if a polypeptide were subjected to treatment with any of the common endopeptidases, such as trypsin or chymotrypsin, the oligopeptides resulting from such treatment would represent portions, segments or fragments of the starting polypeptide. When used in relation to a polynucleotide, such terms refer to the products produced by treatment of said polynucleotides with any of the common endonucleases, or any stretch of polynucleotides that could be synthetically synthesized.

As used herein, the term "DNA segment" or "DNA sequence" refers to a DNA polymer, in the form of a separate fragment or as a component of a larger DNA construct, which has been derived from DNA, and may include both single stranded and duplex sequences. Such segments are provided in the form of an open reading frame uninterrupted by internal non-translated sequences, or introns, which are typically present in eukaryotic genes.

20

The term "coding region" refers to that portion of a gene which either naturally or normally codes for the expression product of that gene in its natural genomic environment, i.e., the region coding *in vivo* for the native expression product of the gene.

25

The term "nucleotide sequence" refers to a heteropolymer of deoxyribonucleotides. Generally, DNA segments encoding the proteins provided by this invention are assembled from cDNA fragments and short oligonucleotide linkers, or from a series of oligonucleotides, to provide a synthetic gene which is capable of being expressed in a recombinant transcriptional unit comprising regulatory elements derived from a microbial or viral operon.

30

The term "expression product" means that polypeptide or protein that is the natural translation product of the gene and any nucleic acid sequence coding equivalents resulting from genetic code degeneracy and thus coding  
5 for the same amino acid(s).

The term "fragment," when referring to a coding sequence, means a portion of DNA comprising less than the complete coding region whose expression product retains essentially the same biological function or activity  
10 as the expression product of the complete coding region.

The present invention also finds use as a means of diagnosing the presence of cancer in a patient, as where a sample of cancerous tissues or cells, or tissues or cells suspected of being cancerous. For such purposes,  
15 and in accordance with the disclosure elsewhere herein, such diagnosis is based on the detection of elevated expression or amplification, such as elevated copy number, of one or more of the genes identified according to the invention. Such elevated expression can be determined by any of the means described herein.

20

In one such embodiment, the elevated expression, as compared to normal cells and/or tissues of the same organ, is determined by measuring the relative rates of transcription of RNA, such as by production of corresponding cDNAs and then analyzing the resulting DNA using probes  
25 developed from the gene sequences as identified in Table 1. Thus, the levels of cDNA produced by use of reverse transcriptase with the full RNA complement of a cell suspected of being cancerous produces a corresponding amount of cDNA that can then be amplified using polymerase chain reaction, or some other means, such as rolling circle amplification, to determine the  
30 relative levels of resulting cDNA and, thereby, the relative levels of gene expression.

For RNA analysis, the latter may be isolated from samples in a variety of ways, including lysis and denaturation with a phenolic solution containing a chaotropic agent (e.g., triazol) followed by isopropanol precipitation, ethanol wash, and resuspension in aqueous solution; or lysis and denaturation  
5 followed by isolation on solid support, such as a Qiagen resin and reconstitution in aqueous solution; or lysis and denaturation in non-phenolic, aqueous solutions followed by enzymatic conversion of RNA to DNA template copies. Steady state RNA levels for a given type of cell or tissue may have to be ascertained prior to employment of the methods of the invention but such  
10 is well within the skill of those in the art and will not be further described in detail herein.

Alternatively, increased expression, such as increased copy number, may be determined for the genes present in a cancerous cell, or a cell  
15 suspected of being cancerous, by using the nucleotides sequences as identified in Table 1 as a means of generating probes for the DNAs present in the cells to be examined. Thus, the DNA of such cells may be extracted and probed using the sequences disclosed herein for the presence in the genomes of such cells of increased amounts of one or more of the genes of  
20 the invention. For example, where a cancer-related, or cancer-linked, gene as disclosed herein is found to be present in multiple copies within the genome of a cell, even where it may not be actively being over-expressed at the time of such determination, this may be indicative of at least a disposition toward developing cancer at a subsequent time.

25

In accordance with the foregoing, the presence of such multiple copies of a gene, or genes, as disclosed herein may be determined using northern or southern blotting and employing the sequences as identified in Table 1 to develop probes for this purpose. Such probes may be composed of DNA or  
30 RNA and may advantageously be comprised of a contiguous stretch of nucleotide residues matching, or complementary to, a sequence as identified in Table 1. Such probes will most usefully comprise a contiguous stretch of at



least 15, preferably at least 30, more preferably at least 50, most preferably at least 80, and especially at least 100, even 200 residues, derived from one or more of the sequences as identified in Table 1. Thus, where a single probe binds multiple times to the genome of a sample of cells that are cancerous, or  
5 are suspected of being cancerous, or predisposed to become cancerous, whereas binding of the same probe to a similar amount of DNA derived from the genome of otherwise non-cancerous cells of the same organ or tissue results in observably less binding, this is indicative of the presence of multiple copies of a gene comprising, or corresponding to, the sequence as identified  
10 in Table 1 from which the probe sequenced was derived.

Increased expression may also be determined using agents that selectively bind to, and thereby detect, the presence of expression products of the genes disclosed herein. For example, an antibody, possibly a suitably  
15 labeled antibody, such as where the antibody is bound to a fluorescent or radiolabel, may be generated against one of the polypeptides comprising a sequence as identified in Table 1 (serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate); for polypeptide SEQ ID NOs, see Table 1, serial number 806-923 (transcript or protein)), and said antibody  
20 will then react with, binding either selectively or specifically, to a polypeptide encoded by one of the genes that corresponds to a sequence disclosed herein. Such antibody binding, especially relative extent of such binding in samples derived from suspected cancerous, as opposed to otherwise non-cancerous, cells and tissues, can then be used as a measure of the extent of  
25 expression, or over-expression, of the cancer-related genes identified herein. Thus, the genes identified herein as being over-expressed in cancerous cells and tissues may be over-expressed due to increased copy number, or due to over-transcription, such as where the over-expression is due to over-production of a transcription factor that activates the gene and leads to  
30 repeated binding of RNA polymerase, thereby generating large than normal amounts of RNA transcripts, which are subsequently translated into polypeptides, such as the polypeptides comprising amino acid sequences as

identified in Table 1 (SEQ ID NO: 1 – 923). Such analysis provides an additional means of ascertaining the expression of the genes identified according to the invention and thereby determining the presence of a cancerous state in a sample derived from a patient to be tested, of the  
5 predisposition to develop cancer at a subsequent time in said patient.

In employing the methods of the invention, it should be borne in mind that gene expression indicative of a cancerous state need not be characteristic of every cell found to be cancerous. Thus, the methods  
10 disclosed herein are useful for detecting the presence of a cancerous condition within a tissue where less than all cells exhibit the complete pattern of over-expression. For example, a set of selected genes, comprising sequences homologous under stringent conditions, or at least 90%, preferably 95%, identical to at least one of the sequences as identified in Table 1, may  
15 be found, using appropriate probes, either DNA or RNA, to be present in as little as 60% of cells derived from a sample of tumorous, or malignant, tissue while being absent from as much as 60% of cells derived from corresponding non-cancerous, or otherwise normal, tissue (and thus being present in as much as 40% of such normal tissue cells). In a preferred embodiment, such  
20 gene pattern is found to be present in at least 70% of cells drawn from a cancerous tissue and absent from at least 70% of a corresponding normal, non-cancerous, tissue sample. In an especially preferred embodiment, such gene pattern is found to be present in at least 80% of cells drawn from a cancerous tissue and absent from at least 80% of a corresponding normal,  
25 non-cancerous, tissue sample. In a most preferred embodiment, such gene pattern is found to be present in at least 90% of cells drawn from a cancerous tissue and absent from at least 90% of a corresponding normal, non-cancerous, tissue sample. In an additional embodiment, such gene pattern is found to be present in at least 100% of cells drawn from a cancerous tissue  
30 and absent from at least 100% of a corresponding normal, non-cancerous, tissue sample, although the latter embodiment may represent a rare occurrence.

In an additional aspect, the present invention relates to a method for determining a cancer initiating or facilitating gene comprising contacting a cell expressing a test gene (i.e., a gene whose status as a cancer initiating or facilitating gene is to be determined) with an agent that decreases the expression of a gene that encodes an RNA at least 90%, preferably 95%, identical to an RNA encoded by (i.e., a gene corresponding to) a polynucleotide comprising, or having, a sequence selected from the group consisting as identified in Table 1 and detecting a decrease in expression of said test gene compared to when said agent is not present, thereby identifying said test gene as being a cancer initiating or facilitating gene. Such genes may, of course, be oncogenes and said decrease in expression may be due to a decrease in copy number of said gene in said cell or a cell derived from said cell, such as where copy number is reduced in the cells formed by replication of such cells.

Thus, some or all of the genes disclosed herein as corresponding to as identified in Table 1 are found to play a direct role in the initiation or progression of cancer or even other diseases and disease processes. Because changes in expression of these genes (up-regulation) are linked to the disease state (i.e. cancer), the change in expression may contribute to the initiation or progression of the disease. For example, if a gene that is up-regulated is an oncogene such a gene provides for a means of screening for small molecule therapeutics beyond screens based upon expression output alone. For example, genes that display up-regulation in cancer and whose elevated expression contributes to initiation or progression of disease represent targets in screens for small molecules that inhibit or block their function. Examples include, but are not be limited to, kinase inhibition, cellular proliferation, substrate analogs that block the active site of protein targets, etc.

It should be noted that there are a variety of different contexts in which genes have been evaluated as being involved in the cancerous process.

Thus, some genes may be oncogenes and encode proteins that are directly involved in the cancerous process and thereby promote the occurrence of cancer in an animal. Other genes may simply be involved either directly or indirectly in the cancerous process or condition and may serve in an ancillary capacity with respect to the cancerous state. All such types of genes are deemed with those to be determined in accordance with the invention as disclosed herein. Thus, the gene determined by said method of the invention may be an oncogene, or the gene determined by said method may be a cancer facilitating gene, the latter including a gene that directly or indirectly affects the cancerous process, either in the promotion of a cancerous condition or in facilitating the progress of cancerous growth or otherwise modulating the growth of cancer cells, either *in vivo* or *ex vivo*. Such genes may work indirectly where their expression alters the activity of some other gene or gene expression product that is itself directly involved in initiating or facilitating the progress of a cancerous condition. For example, a gene that encodes a polypeptide, either wild or mutant in type, which polypeptide acts to suppress of tumor suppressor gene, or its expression product, will thereby act indirectly to promote tumor growth.

In accordance with the foregoing, the method of the present invention includes cancer modulating agents that are themselves either polypeptides, or small chemical entities, that affect the cancerous process, including initiation, suppression or facilitation of tumor growth, either *in vivo* or *ex vivo*. Such agents may also be antibodies that react with one or more of the polypeptides as identified in Table 1 ((SEQ ID NO: 806-923 (transcript or protein))).

In keeping with the disclosure herein, the present invention also relates to a method for treating cancer comprising contacting a cancerous cell with an agent having activity against an expression product encoded by a gene mapping within regions of chromosomal interest or, alternatively, a gene corresponding to a polynucleotide that comprises a nucleotide sequence as

identified in Table 1, such as where such expression product is one the polypeptides as identified in Table 1.

5 The method of the present invention includes embodiments of the above-recited method wherein said cancer cell is contacted *in vivo* as well as *ex vivo*, preferably wherein said agent comprises a portion, or is part of an overall molecular structure, having affinity for said expression product. In one such embodiment, said portion having affinity for said expression product is an antibody.

10

In one embodiment of the present invention, a chemical agent, such as a protein or other polypeptide, is joined to an agent, such as an antibody, having affinity for an expression product of a cancerous cell, such as a polypeptide or protein encoded by a gene related to the cancerous process, especially a gene sequence corresponding to one of the cDNA sequences as identified in Table 1. In a specific embodiment, said expression product acts as a therapeutic target for the affinity portion of said anticancer agent and where, after binding of the affinity portion of such agent to the expression product, the anti-cancer portion of said agent acts against said expression product so as to neutralize its effects in initiating, facilitating or promoting tumor formation and/or growth. In a separate embodiment of the present invention, binding of the agent to said expression product may, without more, have the effect of deterring cancer promotion, facilitation or growth, especially where the presence of said expression product is related, either intimately or only in an ancillary manner, to the development and growth of a tumor. Thus, where the presence of said expression product is essential to tumor initiation and/or growth, binding of said agent to said expression product will have the effect of negating said tumor promoting activity. In one such embodiment, said agent is an apoptosis-inducing agent that induces cell suicide, thereby killing the cancer cell and halting tumor growth.

30

Many cancers contain chromosomal rearrangements, which typically represent translocations, amplifications, or deletions of specific regions of genomic DNA. A recurrent chromosomal rearrangement that is associated with a specific stage and type of cancer always affects a gene (or possibly  
5 genes) that play a direct and critical role in the initiation or progression of the disease. Many of the known oncogenes or tumor suppressor genes that play direct roles in cancer have either been initially identified based upon their positional cloning from a recurrent chromosomal rearrangement or have been demonstrated to fall within a rearrangement subsequent to their cloning by  
10 other methods. In all cases, such genes display amplification at both the level of DNA copy number and at the level of transcriptional expression at the mRNA level.

The present method also relates to a method for determining  
15 functionally related genes comprising contacting one or more gene sequences corresponding to the cDNAs as identified in Table 1 with an agent that modulates expression of more than one gene in such group and thereby determining a subset of genes of said group.

20 In accordance with the present invention, said functionally related genes are genes modulating the same metabolic pathway or said genes are genes encoding functionally related polypeptides. In one such embodiment, said genes are genes whose expression is modulated by the same transcriptional activator or enhancer sequence, especially where said  
25 transcriptional activator or enhancer increases, or otherwise modulates, the activity of a gene corresponding to a cDNA as identified in Table 1.

The present invention also relates to a process that comprises a method for producing a product comprising identifying an agent according to  
30 one of the disclosed methods for identifying such an agent (i.e., the therapeutic agents identified according to the assay procedures disclosed herein) wherein said product is the data collected with respect to said agent

as a result of said identification process, or assay, and wherein said data is sufficient to convey the chemical character and/or structure and/or properties of said agent. For example, the present invention specifically contemplates a situation whereby a user of an assay of the invention may use the assay to  
5 screen for compounds having the desired enzyme modulating activity and, having identified the compound, then conveys that information (i.e., information as to structure, dosage, etc) to another user who then utilizes the information to reproduce the agent and administer it for therapeutic or research purposes according to the invention. For example, the user of the  
10 assay (user 1) may screen a number of test compounds without knowing the structure or identity of the compounds (such as where a number of code numbers are used the first user is simply given samples labeled with said code numbers) and, after performing the screening process, using one or more assay processes of the present invention, then imparts to a second user  
15 (user 2), verbally or in writing or some equivalent fashion, sufficient information to identify the compounds having a particular modulating activity (for example, the code number with the corresponding results). This transmission of information from user 1 to user 2 is specifically contemplated by the present invention.

20

In accordance with the foregoing, the present invention relates to a method for producing test data with respect to the anti-neoplastic activity of a compound comprising:

(a) contacting a compound with a cell that expresses at least one gene  
25 corresponding to a polynucleotide comprising a nucleotide sequence of serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate) of Table 1 or encoding a polypeptide or transcript of SEQ ID NO: 806-923 and under conditions promoting expression of said gene;

(b) detecting a change in expression of said gene compared to  
30 expression when said compound is not present; and

(c) producing test data with respect to the gene modulating activity of said compound based on a change in the expression of the determined gene,

or genes, whose expression is otherwise elevated in a non-cancerous cell over that in a cancerous cell and a decrease in the expression of the determined gene, or genes whose expression is otherwise increased in a cancerous cell over that in a non-cancerous cell indicating anti-neoplastic activity.

In another embodiment, the present invention provides a method for monitoring the progress of a cancer treatment, such as where the methods of the invention permit a determination that a given course of cancer therapy is or is not proving effective because of an increased or decreased expression of a gene, or genes, disclosed herein. For example, where there is an increased copy number of one or more of the genes as identified in Table 1 (SEQ ID NO: 1 – 805), monitoring of such genes can predict success or failure of a course of therapy, such as chemotherapy, or predict the likelihood of a relapse based on elevated activity or expression of one or more of these genes following such course of therapy.

In accordance with the foregoing, the present invention contemplates a method for determining the progress of a treatment for cancer in a patient afflicted with cancer, following commencement of a cancer treatment on said patient, comprising:

(a) determining in said patient a change in expression of one or more genes corresponding to a polynucleotide comprising a nucleotide sequence of serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate) of Table 1 or encoding a polypeptide or transcript of serial number 806-923 of Table 1 (which include any of SEQ ID NO: 1 – 923) and under conditions promoting expression of said one or more genes; and

(b) detecting a change in expression of said gene compared to expression of said one or more determined genes prior to commencement of said cancer treatment;

thereby determining the progress of said treatment.



In a preferred embodiment, the detected change in expression is a decrease in expression. In another preferred embodiment, the cancer treatment is treatment with a chemotherapeutic agent, especially an agent that modulates, preferably decreases, expression of a gene identified herein, such as where said agent was first identified as having anti-neoplastic activity using a method of the invention. Thus, in accordance with this aspect of the present invention, a patient, or even a research animal, such as a mouse, rat, rabbit or primate, afflicted with cancer, including a cancer induced for research purposes, is introduced to a cancer treatment regimen, such as administration of an anti-cancer agent, including one first identified as having anti-neoplastic activity by one or more of the screening methods disclosed herein. The progress and success or failure of such treatment is subsequently ascertained by determining the subsequent expression of one or more, preferably at least 3, or 5, or 10, of the genes identified herein, or that encodes a transcript or polypeptide disclosed herein (see Table 1) following said treatment. In a preferred embodiment, a treatment that reduces said expression is deemed advantageous and may then be the basis for continuing said treatment. The methods of the invention thereby provide a means of continually monitoring the success of the treatment and evaluating both the need, and desirability, of continuing said treatment. In addition, more than one said treatment may be administered simultaneously without diminishing the value of the methods of the invention in determining the overall success of such combined treatment. Thus, more than one said anti-neoplastic agent may be administered to the same patient and overall effectiveness ascertained by the recited methods.

In accordance with the foregoing, the present invention also contemplates a method for determining the likelihood of survival of a patient afflicted with cancer, following commencement of a cancer treatment on said patient, comprising:

(a) determining in said patient a change in expression of one or more genes corresponding to a polynucleotide comprising a nucleotide sequence of

serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate) of Table 1 or encoding a polypeptide or transcript of serial number 806-923 of Table 1 and under conditions promoting expression of said one or more genes; and

- 5 (b) detecting a change in expression of said gene compared to expression of said one or more determined genes prior to commencement of said cancer treatment;

thereby determining the likelihood of survival of said treatment.

- 10 In a preferred embodiment, the detected change in expression is a decrease in expression and said determined gene, or genes, may include 2, 3, 5, 10 or more of the genes described herein. Thus, the methods of the invention may be utilized as a means for compiling cancer survival statistics following one or more, possibly combined, treatments for cancer as in keeping  
15 with the other methods disclosed herein.

- The genes identified herein also offer themselves as pharmacodynamic markers (or as pharmacogenetic and/or surrogate markers), such as for patient profiling prior to clinical trials and/or targeted therapies, including  
20 combination treatments, resulting from the identification of these genes as valid gene targets for chemotherapy based on the screening procedures of the invention. In one embodiment thereof, the likelihood of success of a cancer treatment with a selected chemotherapeutic agent may be based on the fact that such agent has been determined to have expression modulating  
25 activity with one or more genes identified herein, especially where said genes have been identified as showing elevated expression levels in samples from a prospective patient afflicted with cancer. Methods described elsewhere herein for determining cancerous status of a cell may find ready use in such evaluations.

- 30 It should be cautioned that, in carrying out the procedures of the present invention as disclosed herein, any reference to particular buffers,

media, reagents, cells, culture conditions and the like are not intended to be limiting, but are to be read so as to include all related materials that one of ordinary skill in the art would recognize as being of interest or value in the particular context in which that discussion is presented. For example, it is often possible to substitute one buffer system or culture medium for another and still achieve similar, if not identical, results. Those of skill in the art will have sufficient knowledge of such systems and methodologies so as to be able, without undue experimentation, to make such substitutions as will optimally serve their purposes in using the methods and procedures disclosed herein.

The present invention will now be further described by way of the following non-limiting example. In applying the disclosure of the example, it should be kept clearly in mind that other and different embodiments of the methods disclosed according to the present invention will no doubt suggest themselves to those of skill in the relevant art.

20

### EXAMPLE

Cancerous cells that over-express one or more of the genes selected from those that correspond to genes as identified in Table 1 (serial number 1-229 (breast), 230-440 (colon), 441-656 (lung) and 657-805 (prostate); serial number 806-923 (transcript or protein), or SEQ ID NO: 1 – 805 and 855 - 923) are grown to a density of  $10^5$  cells/cm<sup>2</sup> in Leibovitz's L-15 medium supplemented with 2 mM L-glutamine (90%) and 10% fetal bovine serum. The cells are collected after treatment with 0.25% trypsin, 0.02% EDTA at 37°C for 2 to 5 minutes. The trypsinized cells are then diluted with 30 ml growth medium and plated at a density of 50,000 cells per well in a 96 well plate (200 µl/well). The following day, cells are treated with either compound buffer alone, or compound buffer containing a chemical agent to be tested, for 24 hours. The media is then removed, the cells lysed and the RNA recovered

using the RNAeasy reagents and protocol obtained from Qiagen. RNA is quantitated and 10 ng of sample in 1  $\mu$ l are added to 24  $\mu$ l of Taqman reaction mix containing 1X PCR buffer, RNAsin, reverse transcriptase, nucleoside triphosphates, amplitaq gold, tween 20, glycerol, bovine serum albumin (BSA) and specific PCR primers and probes for a reference gene (18S RNA) and a test gene (Gene X). Reverse transcription is then carried out at 48°C for 30 minutes. The sample is then applied to a Perlin Elmer 7700 sequence detector and heat denatured for 10 minutes at 95°C. Amplification is performed through 40 cycles using 15 seconds annealing at 60°C followed by a 60 second extension at 72°C and 30 second denaturation at 95°C. Data files are then captured and the data analyzed with the appropriate baseline windows and thresholds.

The quantitative difference between the target and reference genes is then calculated and a relative expression value determined for all of the samples used. This procedure is then repeated for each of the target genes in a given signature, or characteristic, set and the relative expression ratios for each pair of genes is determined (i.e., a ratio of expression is determined for each target gene versus each of the other genes for which expression is measured, where each gene's absolute expression is determined relative to the reference gene for each compound, or chemical agent, to be screened). The samples are then scored and ranked according to the degree of alteration of the expression profile in the treated samples relative to the control. The overall expression of the set of genes relative to the controls, as modulated by one chemical agent relative to another, is also ascertained. Chemical agents having the most effect on a given gene, or set of genes, are considered the most anti-neoplastic.

Table 1

Serial No.	SEQ ID	accession	tissue	p_m	chr	band	unigene	Description	Protein/ Transcript
1	3	AK000490	breast	primary	1	p31.2	Hs.133260	hypothetical protein FLJ20354	
2	10	R33352	breast	primary	1	p31.3	NULL	unknown	
3	13	AI739473	breast	primary	1	p32.3	Hs.75616	24-dehydrocholesterol reductase	
4	5	U63743	breast	primary	1	p34.1	Hs.69360	kinesin-like 6 (mitotic centromere-associated kinesin)	
5	2	U05340	breast	primary	1	p34.2	Hs.82906	CDC20 cell division cycle 20 homolog (S. cerevisiae)	
6	11	AA203213	breast	primary	1	p36.33	Hs.833	interferon-stimulated protein 15 kDa	
7	12	T16144	breast	primary	1	q21.3	NULL	unknown	
8	1	AI053741	breast	primary	1	q22	Hs.133294	ESTs	
9	14	AB037776	breast	primary	1	q23.1	Hs.38002	immunoglobulin superfamily member 9	
10	9	AA830844	breast	primary	1	q23.2	Hs.127310	kinase interacting with leukemia-associated gene (stathmin)	
11	7	AF326731	breast	primary	1	q23.3	Hs.234545	cell division cycle associated 1	
12	4	AB032931	breast	primary	1	q32.1	Hs.5199	HSPC150 protein similar to ubiquitin-conjugating enzyme	
13	8	AI380204	breast	primary	1	q32.1	Hs.118064	similar to rat nuclear ubiquitous casein kinase 2	
14	6	U30872	breast	primary	1	q32.3	Hs.77204	centromere protein F 350/400ka (mitosin)	
15	55	U14518	breast	primary	2	p23.3	Hs.1594	centromere protein A 17kDa	
16	54	AI492879	breast	primary	2	p25.1	Hs.75319	ribonucleotide reductase M2 polypeptide	
17	56	AL045632	breast	primary	2	q33.1	Hs.44269	hypothetical protein FLJ25211	
18	74	M86699	breast	primary	3	p21.31	Hs.169840	TTK protein kinase	
19	77	AI962335	breast	primary	3	p24.3	Hs.196042	ESTs	
20	75	AI867102	breast	primary	3	p25.1	Hs.56966	KIAA0906 protein	
21	71	AI751438	breast	primary	3	q12.3	Hs.41271	Homo sapiens mRNA full length insert cDNA clone EUROIIMAGE 1913076	

Table 1 (Continued)

22	72	X57527	breast	primary	3	q12.3	Hs.114599	collagen type VIII alpha 1
23	76	W02608	breast	primary	3	q26.1	Hs.36830	ESTs Moderately similar to zinc finger protein 91 (HPF7 HTF10) [Homo sapiens] [H.sapiens]
24	73	A1823992	breast	primary	3	q26.32	Hs.122579	epithelial cell transforming sequence 2 oncogene
25	78	A1087975	breast	primary	3	q28	Hs.195225	ESTs
26	82	AW001872	breast	primary	5	p13.1	Hs.58435	FYN binding protein (FYB-120/130)
27	80	BE407516	breast	primary	5	q13.2	Hs.23960	cyclin B1
28	81	U70370	breast	primary	5	q31.1	Hs.84136	paired-like homeodomain transcription factor 1
29	79	A1739117	breast	primary	5	q31.2	Hs.73625	RAB6 interacting kinesin-like (rabkinesin6)
30	83	D14678	breast	primary	6	p21.32	Hs.20830	kinesin-like 2
31	85	M13436	breast	primary	7	p14.1	Hs.727	inhibin beta A (activin A activin AB alpha polypeptide)
32	86	A1343467	breast	primary	7	p14.1	Hs.28792	Homo sapiens cDNA FLJ11041 fis clone PLACE1004405
33	84	AK023208	breast	primary	7	p14.2	Hs.62180	anillin actin binding protein (scraps homolog Drosophila)
34	89	A1285531	breast	primary	7	p15.2	Hs.106260	sorting nexin 10
35	87	A1922323	breast	primary	7	p21.1	Hs.91011	anterior gradient 2 homolog (Xenopus laevis)
36	88	U61145	breast	primary	7	q36.1	Hs.77256	enhancer of zeste homolog 2 (Drosophila)
37	99	AA625199	breast	primary	8	NULL	Hs.352415	solute carrier family 39 (zinc transporter) member 4
38	100	A1949095	breast	primary	8	NULL	Hs.67776	Homo sapiens clone IMAGE:5455669 mRNA partial cds
39	90	A1932328	breast	primary	8	p21.1	Hs.104741	T-LAK cell-originated protein kinase
40	91	AA203476	breast	primary	8	q13.2	Hs.252587	pituitary tumor-transforming 1
41	92	AW043713	breast	primary	8	q13.3	Hs.70823	sulfatase FP
42	96	BE974098	breast	primary	8	q21.13	Hs.2384	tumor protein D52
43	98	AF091433	breast	primary	8	q22.1	Hs.30464	cyclin E2
44	95	AA046853	breast	primary	8	q24.12	Hs.76550	mal T-cell differentiation protein 2
45	93	A1925583	breast	primary	8	q24.13	Hs.222088	hypothetical protein MGC5254
46	97	AF098865	breast	primary	8	q24.13	Hs.71465	squalene epoxidase

Table 1 (Continued)

47	94	AA147884	breast	primary	8	q24.22	Hs.9812	Homo sapiens cDNA FLJ14388 fis clone HEMBA1002716
48	103	AW007586	breast	primary	9	q34.11	Hs.133122	zinc finger DHHC domain containing 12
49	101	W25552	breast	primary	9	q34.3	Hs.212613	hypothetical protein FLJ36779
50	102	AI811865	breast	primary	9	q34.3	Hs.274152	EST
51	17	AF067656	breast	primary	10	q21.1	Hs.42650	ZW10 interactor
52	16	AL524035	breast	primary	10	q21.2	Hs.334562	cell division cycle 2 G1 to S and G2 to M
53	15	AI674163	breast	primary	10	q23.33	Hs.14559	hypothetical protein FLJ10540
54	21	AB018293	breast	primary	11	p15.3	Hs.314434	KIAA0750 gene product
55	18	AL079372	breast	primary	11	q13.1	Hs.23044	similar to RIKEN cDNA 2610036L13
56	22	D60944	breast	primary	11	q13.4	Hs.84700	serologically defined colon cancer antigen 28
57	19	X14850	breast	primary	11	q23.3	Hs.147097	H2A histone family member X
58	20	AA704137	breast	primary	11	q23.3	Hs.125359	Thy-1 cell surface antigen
59	23	U74612	breast	primary	12	p13.33	Hs.239	forkhead box M1
60	24	U82984	breast	primary	12	q13.12	Hs.23900	Rac GTPase activating protein 1
61	25	AI291142	breast	primary	13	q33.3	Hs.183874	culin 4A
62	26	L25876	breast	primary	14	q22.1	Hs.84113	cyclin-dependent kinase inhibitor 3 (CDK2-associated dual specificity phosphatase)
63	27	AL080146	breast	primary	15	q21.3	Hs.194698	cyclin B2
64	28	D14657	breast	primary	15	q22.2	Hs.81892	KIAA0101 gene product
65	29	AA195614	breast	primary	15	q25.3	Hs.344037	protein regulator of cytokinesis 1
66	31	AW003626	breast	primary	16	NULL	Hs.159154	tubulin beta 4
67	32	BC003186	breast	primary	16	NULL	Hs.108196	HSPC037 protein
68	30	AI819340	breast	primary	16	p13.3	Hs.13561	hypothetical protein MGC4692
69	34	W92110	breast	primary	16	p13.3	Hs.279623	selenoprotein X 1
70	35	AI953838	breast	primary	16	p13.3	Hs.124015	hypothetical protein MGC2605
71	36	AL520675	breast	primary	16	p13.3	Hs.351474	hypothetical protein FLJ30002
72	37	BE965311	breast	primary	16	p13.3	Hs.124915	hypothetical protein MGC2601
73	38	AI701742	breast	primary	16	p13.3	Hs.290943	Homo sapiens similar to possible G-protein receptor clone MGC:21993 IMAGE:4398317
74	33	AA904482	breast	primary	16	q12.2	Hs.368078	mRNA complete cds ESTs

Table 1 (Continued)

75	42	AI683036	breast	primary	17	NULL	Hs.314169	KIAA1618 protein
76	44	U81800	breast	primary	17	NULL	Hs.85838	solute carrier family 16 (monocarboxylic acid transporters) member 3
77	45	BE328850	breast	primary	17	q11.2	Hs.348504	hypothetical protein BC014072
78	39	AW003286	breast	primary	17	q21.31	Hs.370428	ESTs Moderately similar to TP2A_HUMAN DNA topoisomerase II alpha isoform [H.sapiens]
79	41	AL561834	breast	primary	17	q21.31	Hs.156346	topoisomerase (DNA) II alpha 170kDa
80	48	L47276	breast	primary	17	q21.31	NULL	unknown
81	49	BC001038	breast	primary	17	q22	Hs.307036	Homo sapiens Similar to epsin 3 clone MGC:1006 IMAGE:3505495 mRNA complete cds
82	40	AA424160	breast	primary	17	q23.2	Hs.165909	ESTs Weakly similar to hypothetical protein FLJ20489 [Homo sapiens] [H.sapiens]
83	51	BF029215	breast	primary	17	q23.2	Hs.103512	Homo sapiens cDNA FLJ36569 fis clone TRACH2010824 highly similar to Ribonucleoprotein
84	43	AI675178	breast	primary	17	q24.2	Hs.90207	hypothetical protein MGC11138
85	50	U28386	breast	primary	17	q24.3	Hs.159557	karyopherin alpha 2 (RAG cohort 1 importin alpha 1)
86	46	AA635844	breast	primary	17	q25.3	Hs.109706	hematological and neurological expressed 1
87	47	K02581	breast	primary	17	q25.3	Hs.105097	thymidine kinase 1 soluble
88	52	AF017790	breast	primary	18	p11.32	Hs.58169	highly expressed in cancer rich in leucine heptad repeats
89	53	AA719022	breast	primary	19	q13.43	Hs.288549	ubiquitin UBF-fl
90	65	D80008	breast	primary	20	p11.21	Hs.36232	KIAA0186 gene product
91	63	AI990405	breast	primary	20	p11.23	Hs.194691	retinoic acid induced 3
92	57	AA534688	breast	primary	20	q11.1	Hs.9329	chromosome 20 open reading frame 1
93	66	AW003586	breast	primary	20	q11.22	Hs.274411	SCAN domain containing 1
94	59	U73379	breast	primary	20	q13.12	Hs.93002	ubiquitin-conjugating enzyme E2C
95	62	AI990026	breast	primary	20	q13.12	Hs.286	ribosomal protein L4
96	67	AA207074	breast	primary	20	q13.13	Hs.56237	breast carcinoma amplified sequence 4



Table 1 (Continued)

97	60	AF041260	breast	primary	20	q13.2	Hs.129057	breast carcinoma amplified sequence 1
98	61	AF011468	breast	primary	20	q13.31	Hs.250822	serine/threonine kinase 6
99	58	AA535819	breast	primary	20	q13.32	Hs.83883	transmembrane prostate androgen induced RNA
100	64	X70940	breast	primary	20	q13.33	Hs.2642	eukaryotic translation elongation factor 1 alpha 2
101	69	Y15915	breast	primary	22	q13.1	Hs.172928	collagen type I alpha 1
102	70	AL035081	breast	primary	22	q13.1	Hs.250696	KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 3
103	68	AI381686	breast	primary	22	q13.2	Hs.208912	hypothetical protein MGC861
104	106	AK000490	breast	metastatic	1	p31.2	Hs.133260	hypothetical protein FLJ20354
105	113	R33352	breast	metastatic	1	p31.3	NULL	unknown
106	116	AI739473	breast	metastatic	1	p32.3	Hs.75616	24-dehydrocholesterol reductase
107	108	U63743	breast	metastatic	1	p34.1	Hs.69360	kinesin-like 6 (mitotic centromere-associated kinesin)
108	105	U05340	breast	metastatic	1	p34.2	Hs.82906	CDC20 cell division cycle 20 homolog (S. cerevisiae)
109	119	AI992172	breast	metastatic	1	p36.13	Hs.83551	microfibrillar-associated protein 2
110	114	AA203213	breast	metastatic	1	p36.33	Hs.833	interferon-stimulated protein 15 kDa
111	115	T16144	breast	metastatic	1	q21.3	NULL	unknown
112	104	AI053741	breast	metastatic	1	q22	Hs.133294	ESTs
113	118	AB037776	breast	metastatic	1	q23.1	Hs.38002	immunoglobulin superfamily member 9
114	112	AA830844	breast	metastatic	1	q23.2	Hs.127310	kinase interacting with leukemia-associated gene (stathmin)
115	120	R62346	breast	metastatic	1	q23.2	NULL	unknown
116	110	AF326731	breast	metastatic	1	q23.3	Hs.234545	cell division cycle associated 1
117	117	AI983896	breast	metastatic	1	q23.3	Hs.191187	ESTs
118	121	AI798144	breast	metastatic	1	q25.2	Hs.209609	ESTs
119	107	AI990409	breast	metastatic	1	q32.1	Hs.5199	HSPC150 protein similar to ubiquitin-conjugating enzyme
120	111	AI380204	breast	metastatic	1	q32.1	Hs.118064	similar to rat nuclear ubiquitous casein kinase 2

Table 1 (Continued)

121	109	U30872	breast	metastatic	1	q32.3	Hs.77204	centromere protein F 350/400ka (mitosin)
122	169	U14518	breast	metastatic	2	p23.3	Hs.1594	centromere protein A 17kDa
123	168	A1492879	breast	metastatic	2	p25.1	Hs.75319	ribonucleotide reductase M2 polypeptide
124	170	AL045632	breast	metastatic	2	q33.1	Hs.44269	hypothetical protein FLJ25211
125	171	N21131	breast	metastatic	2	q37.3	Hs.42949	hairly and enhancer of split 6 (Drosophila)
126	191	M86699	breast	metastatic	3	p21.31	Hs.169840	TTK protein kinase
127	197	AA663786	breast	metastatic	3	p21.31	NULL	unknown
128	194	AI962335	breast	metastatic	3	p24.3	Hs.196042	ESTs
129	195	AB020713	breast	metastatic	3	p25.1	Hs.56966	KIAA0906 protein
130	188	AI557210	breast	metastatic	3	q12.3	Hs.41271	Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 1913076
131	189	X57527	breast	metastatic	3	q12.3	Hs.114599	collagen type VIII alpha 1
132	192	W02608	breast	metastatic	3	q26.1	Hs.36830	ESTs Moderately similar to zinc finger protein 91 (HPF7 HTF10) [Homo sapiens] [H.sapiens]
133	193	AI760298	breast	metastatic	3	q26.31	Hs.128773	ESTs
134	190	AI823992	breast	metastatic	3	q26.32	Hs.122579	epithelial cell transforming sequence 2 oncogene
135	196	AI087975	breast	metastatic	3	q28	Hs.195225	ESTs
136	201	AW001872	breast	metastatic	5	p13.1	Hs.58435	FYN binding protein (FYB-120/130)
137	199	N90191	breast	metastatic	5	q13.2	Hs.23960	cyclin B1
138	200	U70370	breast	metastatic	5	q31.1	Hs.84136	paired-like homeodomain transcription factor 1
139	198	AI739117	breast	metastatic	5	q31.2	Hs.73625	RAB6 interacting kinesin-like (rabkinesin6)
140	202	D14678	breast	metastatic	6	p21.32	Hs.20830	kinesin-like 2
141	204	M13436	breast	metastatic	7	p14.1	Hs.727	inhibin beta A (activin A activin AB alpha polypeptide)
142	205	AA059458	breast	metastatic	7	p14.1	Hs.28792	Homo sapiens cDNA FLJ11041 fis clone PLACE1004405
143	203	AK023208	breast	metastatic	7	p14.2	Hs.62180	anillin actin binding protein (scraps homolog Drosophila)
144	211	AI742239	breast	metastatic	7	p15.1	Hs.91109	Homo sapiens Similar to RIKEN cDNA E130201N16 gene clone IMAGE:3845782 mRNA

Table 1 (Continued)

145	208	AI285531	breast	metastatic	7	p15.2	Hs.106260	sorting nexin 10
146	206	AI922323	breast	metastatic	7	p21.1	Hs.91011	anterior gradient 2 homolog (Xenopus laevis)
147	209	AI961907	breast	metastatic	7	q21.3	Hs.179573	collagen type I alpha 2
148	210	L37127	breast	metastatic	7	q22.1	Hs.80475	polymerase (RNA) II (DNA directed)
								polypeptide J 13.3kDa
149	207	U61145	breast	metastatic	7	q36.1	Hs.77256	enhancer of zeste homolog 2 (Drosophila)
150	220	AA625199	breast	metastatic	8	NULL	Hs.352415	solute carrier family 39 (zinc transporter)
								member 4
151	223	AI949095	breast	metastatic	8	NULL	Hs.67776	Homo sapiens clone IMAGE:5455669 mRNA
								partial cds
152	224	W22510	breast	metastatic	8	NULL	Hs.346950	cellular retinoic acid binding protein 1
153	225	AA292431	breast	metastatic	8	NULL	Hs.92679	kinesin family member C2-like
154	226	AI917311	breast	metastatic	8	NULL	Hs.149152	rhophilin 1
155	212	AI932328	breast	metastatic	8	p21.1	Hs.104741	T-LAK cell-originated protein kinase
156	213	AA203476	breast	metastatic	8	q13.2	Hs.252587	pituitary tumor-transforming 1
157	215	BE500977	breast	metastatic	8	q13.3	Hs.70823	sulfatase FP
158	217	BE974098	breast	metastatic	8	q21.13	Hs.2384	tumor protein D52
159	219	AF091433	breast	metastatic	8	q22.1	Hs.30464	cyclin E2
160	222	AA610522	breast	metastatic	8	q24.11	Hs.162697	ESTs
161	216	AA046853	breast	metastatic	8	q24.12	Hs.76550	mal T-cell differentiation protein 2
162	218	AI656807	breast	metastatic	8	q24.13	Hs.222088	hypothetical protein MGC5254
163	221	D78130	breast	metastatic	8	q24.13	Hs.71465	squalene epoxidase
164	214	AA147884	breast	metastatic	8	q24.22	Hs.9812	Homo sapiens cDNA FLJ14388 fis clone HEMBA1002716
165	229	AW007586	breast	metastatic	9	q34.11	Hs.133122	zinc finger DHHC domain containing 12
166	227	W25552	breast	metastatic	9	q34.3	Hs.212613	hypothetical protein FLJ36779
167	228	AI811865	breast	metastatic	9	q34.3	Hs.274152	EST
168	124	AF067656	breast	metastatic	10	q21.1	Hs.42650	ZW10 interactor
169	123	D88357	breast	metastatic	10	q21.2	Hs.334562	cell division cycle 2 G1 to S and G2 to M
170	122	AI674163	breast	metastatic	10	q23.33	Hs.14559	hypothetical protein FLJ10540
171	125	U37426	breast	metastatic	10	q23.33	Hs.8878	kinesin-like 1
172	131	AA705015	breast	metastatic	11	p15.1	Hs.185918	Homo sapiens cDNA FLJ32525 fis clone

Table 1 (Continued)

173	129	AB018293	breast	metastatic	11	p15.3	Hs.314434	SMINT2000060
174	126	AL079372	breast	metastatic	11	q13.1	Hs.23044	KIAA0750 gene product
175	130	AF151810	breast	metastatic	11	q13.4	Hs.84700	similar to RIKEN cDNA 2610036L13
176	127	X14850	breast	metastatic	11	q23.3	Hs.147097	serologically defined colon cancer antigen 28
177	128	AA704137	breast	metastatic	11	q23.3	Hs.125359	H2A histone family member X
178	132	U74612	breast	metastatic	12	p13.33	Hs.239	Thy-1 cell surface antigen
179	133	U82984	breast	metastatic	12	q13.12	Hs.23900	forkhead box M1
180	134	R61322	breast	metastatic	12	q24.31	Hs.204166	Rac GTPase activating protein 1
181	135	AI291142	breast	metastatic	13	q33.3	Hs.183874	Human clone 295 5cM region surrounding
182	136	L25876	breast	metastatic	14	q22.1	Hs.84113	hepatocyte nuclear factor-1a/MODY3 mRNA
183	137	AL080146	breast	metastatic	15	q21.3	Hs.194698	culin 4A
184	138	D14657	breast	metastatic	15	q22.2	Hs.81892	cyclin-dependent kinase inhibitor 3 (CDK2-
185	139	AA195614	breast	metastatic	15	q25.3	Hs.344037	associated dual specificity phosphatase)
186	141	AW003626	breast	metastatic	16	NULL	Hs.159154	cyclin B2
187	142	BC003186	breast	metastatic	16	NULL	Hs.108196	KIAA0101 gene product
188	149	AI766311	breast	metastatic	16	p12.3	Hs.289047	protein regulator of cytokinesis 1
189	151	AI344053	breast	metastatic	16	p12.3	Hs.115838	tubulin beta 4
190	140	AI819340	breast	metastatic	16	p13.3	Hs.13561	HSPC037 protein
191	144	W92110	breast	metastatic	16	p13.3	Hs.279623	Homo sapiens cDNA FLJ14059 fis clone
192	145	AI953838	breast	metastatic	16	p13.3	Hs.124015	HEMBB1000573
193	146	AL520675	breast	metastatic	16	p13.3	Hs.351474	ESTs Highly similar to hypothetical protein
194	147	BE965311	breast	metastatic	16	p13.3	Hs.124915	FLJ13593 [Homo sapiens] [H.sapiens]
195	148	AI701742	breast	metastatic	16	p13.3	Hs.290943	hypothetical protein MGC4692
196	150	AI655799	breast	metastatic	16	p13.3	Hs.197114	selenoprotein X 1
197	143	AA904482	breast	metastatic	16	q12.2	Hs.368078	hypothetical protein MGC2605
								hypothetical protein FLJ30002
								hypothetical protein MGC2601
								Homo sapiens similar to possible G-protein
								receptor clone MGC:21993 IMAGE:4398317
								mRNA complete cds
								serine/arginine repetitive matrix 2
								ESTs

Table 1 (Continued)

198	154	AI683036	breast	metastatic	17	NULL	Hs.314169	KIAA1618 protein
199	156	U81800	breast	metastatic	17	NULL	Hs.85838	solute carrier family 16 (monocarboxylic acid transporters) member 3
200	157	BE328850	breast	metastatic	17	q11.2	Hs.348504	hypothetical protein BC014072
201	152	AW003286	breast	metastatic	17	q21.31	Hs.370428	ESTs Moderately similar to TP2A_HUMAN
202	158	AI375913	breast	metastatic	17	q21.31	Hs.156346	DNA topoisomerase II alpha isozyme [H.sapiens]
203	161	L47276	breast	metastatic	17	q21.31	NULL	topoisomerase (DNA) II alpha 170kDa unknown
204	162	BC001038	breast	metastatic	17	q22	Hs.307036	Homo sapiens Similar to epsin 3 clone MGC:1006 IMAGE:3505495 mRNA complete cds
205	153	AA424160	breast	metastatic	17	q23.2	Hs.165909	ESTs Weakly similar to hypothetical protein FLJ20489 [Homo sapiens] [H.sapiens]
206	164	BF029215	breast	metastatic	17	q23.2	Hs.103512	Homo sapiens cDNA FLJ36569 fis clone TRACH2010824 highly similar to Ribonucleoprotein
207	155	AI675178	breast	metastatic	17	q24.2	Hs.90207	hypothetical protein MGC11138
208	163	U28386	breast	metastatic	17	q24.3	Hs.159557	karyopherin alpha 2 (RAG cohort 1 importin alpha 1)
209	165	N42752	breast	metastatic	17	q24.3	Hs.42645	ESTs
210	159	K02581	breast	metastatic	17	q25.3	Hs.105097	thymidine kinase 1 soluble
211	160	AI525822	breast	metastatic	17	q25.3	Hs.109706	hematological and neurological expressed 1
212	166	AF017790	breast	metastatic	18	p11.32	Hs.58169	highly expressed in cancer rich in leucine heptad repeats
213	167	AA719022	breast	metastatic	19	q13.43	Hs.288549	ubiquitin UBF-fl
214	180	D80008	breast	metastatic	20	p11.21	Hs.36232	KIAA0186 gene product
215	178	AI990405	breast	metastatic	20	p11.23	Hs.194691	retinoic acid induced 3
216	177	AF098158	breast	metastatic	20	q11.1	Hs.9329	chromosome 20 open reading frame 1
217	181	AW003586	breast	metastatic	20	q11.22	Hs.274411	SCAN domain containing 1
218	173	U73379	breast	metastatic	20	q13.12	Hs.93002	ubiquitin-conjugating enzyme E2C
219	176	AI990026	breast	metastatic	20	q13.12	Hs.286	ribosomal protein L4

Table 1 (Continued)

220	182	AA207074	breast	metastatic	20	q13.13	Hs.56237	breast carcinoma amplified sequence 4
221	174	AF041260	breast	metastatic	20	q13.2	Hs.129057	breast carcinoma amplified sequence 1
222	183	AI638036	breast	metastatic	20	q13.2	Hs.189095	sa-like 4 (Drosophila)
223	175	AF011468	breast	metastatic	20	q13.31	Hs.250822	serine/threonine kinase 6
224	172	AA535819	breast	metastatic	20	q13.32	Hs.83883	transmembrane prostate androgen induced RNA
225	179	X70940	breast	metastatic	20	q13.33	Hs.2642	eukaryotic translation elongation factor 1 alpha
226	184	AI872267	breast	metastatic	20	q13.33	Hs.224895	ESTs
227	186	Y15915	breast	metastatic	22	q13.1	Hs.172928	collagen type I alpha 1
228	187	AL035081	breast	metastatic	22	q13.1	Hs.250696	KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 3
229	185	AI961206	breast	metastatic	22	q13.2	Hs.208912	hypothetical protein MGC861
230	241	AK000490	colon	primary	1	p31.2	Hs.133260	hypothetical protein FLJ20354
231	235	R33352	colon	primary	1	p31.3	NULL	unknown
232	233	AI739473	colon	primary	1	p32.3	Hs.75616	24-dehydrocholesterol reductase
233	239	U63743	colon	primary	1	p34.1	Hs.69360	kinesin-like 6 (mitotic centromere-associated kinesin)
234	243	U05340	colon	primary	1	p34.2	Hs.82906	CDC20 cell division cycle 20 homolog (S. cerevisiae)
235	242	AI990026	colon	primary	1	p35.3	Hs.286	ribosomal protein L4
236	234	T16144	colon	primary	1	q21.3	NULL	unknown
237	232	AW271106	colon	primary	1	q22	Hs.133294	ESTs
238	230	AB037776	colon	primary	1	q23.1	Hs.38002	immunoglobulin superfamily member 9
239	236	AA830844	colon	primary	1	q23.2	Hs.127310	kinase interacting with leukemia-associated gene (statthmin)
240	231	AA383718	colon	primary	1	q23.3	Hs.234545	cell division cycle associated 1
241	237	AI380204	colon	primary	1	q32.1	Hs.118064	similar to rat nuclear ubiquitous casein kinase 2
242	240	AI990409	colon	primary	1	q32.1	Hs.5199	HSPC150 protein similar to ubiquitin-conjugating enzyme
243	238	U30872	colon	primary	1	q32.3	Hs.77204	centromere protein F 350/400ka (mitosin)

Table 1 (Continued)

244	284	U14518	colon	primary	2	p23.3	Hs.1594	centromere protein A 17kDa
245	285	BE966236	colon	primary	2	p25.1	Hs.75319	ribonucleotide reductase M2 polypeptide
246	283	AL045632	colon	primary	2	q33.1	Hs.44269	hypothetical protein FLJ25211
247	302	M86699	colon	primary	3	p21.31	Hs.169840	TTK protein kinase
248	301	AI962335	colon	primary	3	p24.3	Hs.196042	ESTs
249	300	AB020713	colon	primary	3	p25.1	Hs.56966	KIAA0906 protein
250	304	X57527	colon	primary	3	q12.3	Hs.114599	collagen type VIII alpha 1
251	305	AI557210	colon	primary	3	q12.3	Hs.41271	Homo sapiens mRNA full length insert cDNA clone EUROIMAGE 1913076
252	303	AI823992	colon	primary	3	q26.32	Hs.122579	epithelial cell transforming sequence 2 oncogene
253	299	AI087975	colon	primary	3	q28	Hs.195225	ESTs
254	307	AW001872	colon	primary	5	p13.1	Hs.58435	FYN binding protein (FYB-120/130)
255	306	M25753	colon	primary	5	q13.2	Hs.23960	cyclin B1
256	308	U70370	colon	primary	5	q31.1	Hs.84136	paired-like homeodomain transcription factor 1
257	309	AI739117	colon	primary	5	q31.2	Hs.73625	RAB6 interacting kinesin-like (rabkinesin6)
258	310	D14678	colon	primary	6	p21.32	Hs.20830	kinesin-like 2
259	313	AA059458	colon	primary	7	p14.1	Hs.28792	Homo sapiens cDNA FLJ11041 fis clone PLACE1004405
260	315	M13436	colon	primary	7	p14.1	Hs.727	inhibin beta A (activin A activin AB alpha polypeptide)
261	314	AI341261	colon	primary	7	p14.2	Hs.62180	anillin actin binding protein (scraps homolog Drosophila)
262	312	AI922323	colon	primary	7	p21.1	Hs.91011	anterior gradient 2 homolog (Xenopus laevis)
263	311	U61145	colon	primary	7	q36.1	Hs.77256	enhancer of zeste homolog 2 (Drosophila)
264	316	AI949095	colon	primary	8	NULL	Hs.67776	Homo sapiens clone IMAGE:5455669 mRNA partial cds
265	318	AA625199	colon	primary	8	NULL	Hs.352415	solute carrier family 39 (zinc transporter) member 4
266	325	AI932328	colon	primary	8	p21.1	Hs.104741	T-LAK cell-originated protein kinase
267	324	AA203476	colon	primary	8	q13.2	Hs.252587	pituitary tumor-transforming 1
268	323	AW043713	colon	primary	8	q13.3	Hs.70823	sulfatase FP

Table 1 (Continued)

269	319	AF091433	colon	primary	8	q22.1	Hs.30464	cyclin E2
270	321	AL117612	colon	primary	8	q24.12	Hs.76550	mal T-cell differentiation protein 2
271	317	D78130	colon	primary	8	q24.13	Hs.71465	squalene epoxidase
272	320	AI656807	colon	primary	8	q24.13	Hs.222088	hypothetical protein MGC5254
273	322	AA147884	colon	primary	8	q24.22	Hs.9812	Homo sapiens cDNA FLJ14388 fis clone HEMBA1002716
274	326	AW007586	colon	primary	9	q34.11	Hs.133122	zinc finger DHHC domain containing 12
275	327	AI811865	colon	primary	9	q34.3	Hs.274152	EST
276	328	W25552	colon	primary	9	q34.3	Hs.212613	hypothetical protein FLJ36779
277	244	AF067656	colon	primary	10	q21.1	Hs.42650	ZW10 interactor
278	245	AL524035	colon	primary	10	q21.2	Hs.334562	cell division cycle 2 G1 to S and G2 to M
279	246	AI674163	colon	primary	10	q23.33	Hs.14559	hypothetical protein FLJ10540
280	248	AB018293	colon	primary	11	p15.3	Hs.314434	KIAA0750 gene product
281	251	AL079372	colon	primary	11	q13.1	Hs.23044	similar to RIKEN cDNA 2610036L13
282	247	D60944	colon	primary	11	q13.4	Hs.84700	serologically defined colon cancer antigen 28
283	249	AA704137	colon	primary	11	q23.3	Hs.125359	Thy-1 cell surface antigen
284	250	X14850	colon	primary	11	q23.3	Hs.147097	H2A histone family member X
285	253	U74612	colon	primary	12	p13.33	Hs.239	forkhead box M1
286	252	U82984	colon	primary	12	q13.12	Hs.23900	Rac GTPase activating protein 1
287	254	AI291142	colon	primary	13	q33.3	Hs.183874	cullin 4A
288	255	L25876	colon	primary	14	q22.1	Hs.84113	cyclin-dependent kinase inhibitor 3 (CDK2-associated dual specificity phosphatase)
289	258	AL080146	colon	primary	15	q21.3	Hs.194698	cyclin B2
290	257	D14657	colon	primary	15	q22.2	Hs.81892	KIAA0101 gene product
291	256	AA195614	colon	primary	15	q25.3	Hs.344037	protein regulator of cytokinesis 1
292	265	BC003186	colon	primary	16	NULL	Hs.108196	HSPC037 protein
293	266	AW003626	colon	primary	16	NULL	Hs.159154	tubulin beta 4
294	259	AI701742	colon	primary	16	p13.3	Hs.290943	Homo sapiens similar to possible G-protein receptor clone MGC:21993 IMAGE:4398317 mRNA complete cds
295	260	BE965311	colon	primary	16	p13.3	Hs.124915	hypothetical protein MGC2601
296	261	AL520675	colon	primary	16	p13.3	Hs.351474	hypothetical protein FLJ30002



Table 1 (Continued)

297	262	AI953838	colon	primary	16	p13.3	Hs.124015	hypothetical protein MGC2605
298	263	W92110	colon	primary	16	p13.3	Hs.279623	selenoprotein X 1
299	267	AI819340	colon	primary	16	p13.3	Hs.13561	hypothetical protein MGC4692
300	264	AA904482	colon	primary	16	q12.2	Hs.368078	ESTs
301	276	U81800	colon	primary	17	NULL	Hs.85838	solute carrier family 16 (monocarboxylic acid transporters) member 3
302	278	AI683036	colon	primary	17	NULL	Hs.314169	KIAA1618 protein
303	275	BE328850	colon	primary	17	q11.2	Hs.348504	hypothetical protein BC014072
304	272	L47276	colon	primary	17	q21.31	NULL	unknown
305	274	AI375913	colon	primary	17	q21.31	Hs.156346	topoisomerase (DNA) II alpha 170kDa
306	280	AW003286	colon	primary	17	q21.31	Hs.370428	ESTs Moderately similar to TP2A_HUMAN
307	271	BC001038	colon	primary	17	q22	Hs.307036	DNA topoisomerase II alpha isozyme [H.sapiens]
308	269	BF029215	colon	primary	17	q23.2	Hs.103512	Homo sapiens Similar to epsin 3 clone MGC:1006 IMAGE:3505495 mRNA complete cds
309	279	BG165011	colon	primary	17	q23.2	Hs.165909	Homo sapiens cDNA FLJ36569 fis clone TRACH2010824 highly similar to Ribonucleoprotein
310	277	AI675178	colon	primary	17	q24.2	Hs.90207	ESTs Weakly similar to hypothetical protein FLJ20489 [Homo sapiens] [H.sapiens]
311	270	U28386	colon	primary	17	q24.3	Hs.159557	hypothetical protein MGC11138
312	268	AI525822	colon	primary	17	q25.3	Hs.109706	karyopherin alpha 2 (RAG cohort 1 importin alpha 1)
313	273	K02581	colon	primary	17	q25.3	Hs.105097	hematological and neurological expressed 1
314	281	AF017790	colon	primary	18	p11.32	Hs.58169	thymidine kinase 1 soluble
315	282	AA719022	colon	primary	19	q13.43	Hs.288549	highly expressed in cancer rich in leucine heptad repeats
316	288	D80008	colon	primary	20	p11.21	Hs.36232	ubiquitin UBF-fl
317	290	AI990405	colon	primary	20	p11.23	Hs.194691	KIAA0186 gene product
318	291	AF098158	colon	primary	20	q11.1	Hs.9329	retinoic acid induced 3
								chromosome 20 open reading frame 1

Table 1 (Continued)

319	287	AW003586	colon	primary	20	q11.22	Hs.274411	SCAN domain containing 1
320	294	U73379	colon	primary	20	q13.12	Hs.93002	ubiquitin-conjugating enzyme E2C
321	286	AA207074	colon	primary	20	q13.13	Hs.56237	breast carcinoma amplified sequence 4
322	293	AF041260	colon	primary	20	q13.2	Hs.129057	breast carcinoma amplified sequence 1
323	292	AF011468	colon	primary	20	q13.31	Hs.250822	serine/threonine kinase 6
324	295	AA535819	colon	primary	20	q13.32	Hs.83883	transmembrane prostate androgen induced RNA
325	289	X70940	colon	primary	20	q13.33	Hs.2642	eukaryotic translation elongation factor 1 alpha 2
326	296	AL035081	colon	primary	22	q13.1	Hs.250696	KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 3
327	297	Y15916	colon	primary	22	q13.1	Hs.172928	collagen type I alpha 1
328	298	AI381686	colon	primary	22	q13.2	Hs.208912	hypothetical protein MGC861
329	420	AK000490	colon	metastatic	1	p31.2	Hs.133260	hypothetical protein FLJ20354
330	354	R33352	colon	metastatic	1	p31.3	NULL	unknown
331	351	AI739473	colon	metastatic	1	p32.3	Hs.75616	24-dehydrocholesterol reductase
332	396	U63743	colon	metastatic	1	p34.1	Hs.69360	kinesin-like 6 (mitotic centromere-associated kinesin)
333	425	U05340	colon	metastatic	1	p34.2	Hs.82906	CDC20 cell division cycle 20 homolog (S. cerevisiae)
334	421	AI990026	colon	metastatic	1	p35.3	Hs.286	ribosomal protein L4
335	352	T16144	colon	metastatic	1	q21.3	NULL	unknown
336	346	AW271106	colon	metastatic	1	q22	Hs.133294	ESTs
337	340	AB037776	colon	metastatic	1	q23.1	Hs.38002	immunoglobulin superfamily member 9
338	357	AA830844	colon	metastatic	1	q23.2	Hs.127310	kinase interacting with leukemia-associated gene (stathmin)
339	330	AF326731	colon	metastatic	1	q23.3	Hs.234545	cell division cycle associated 1
340	341	AI983896	colon	metastatic	1	q23.3	Hs.191187	ESTs
341	380	AF326731	colon	metastatic	1	q23.3	Hs.234545	cell division cycle associated 1
342	360	AI380204	colon	metastatic	1	q32.1	Hs.118064	similar to rat nuclear ubiquitously casein kinase 2
343	403	AI990409	colon	metastatic	1	q32.1	Hs.5199	HSPC150 protein similar to ubiquitin-

Table 1 (Continued)

344	382	U30872	colon	metastatic	1	q32.3	Hs.77204	conjugating enzyme
345	400	U14518	colon	metastatic	2	p23.3	Hs.1594	centromere protein F 350/400ka (mitosin)
346	419	BE966236	colon	metastatic	2	p25.1	Hs.75319	centromere protein A 17kDa
347	349	AL045632	colon	metastatic	2	q33.1	Hs.44269	ribonucleotide reductase M2 polypeptide
348	365	M86699	colon	metastatic	3	p21.31	Hs.169840	hypothetical protein FLJ25211
349	334	AI962335	colon	metastatic	3	p24.3	Hs.196042	TTK protein kinase
350	333	AB020713	colon	metastatic	3	p25.1	Hs.56966	ESTs
351	412	X57527	colon	metastatic	3	q12.3	Hs.114599	KIAA0906 protein
352	417	AI557210	colon	metastatic	3	q12.3	Hs.41271	collagen type VIII alpha 1
353	344	W02608	colon	metastatic	3	q26.1	Hs.36830	Homo sapiens mRNA full length insert cDNA
354	395	AI823992	colon	metastatic	3	q26.32	Hs.122579	clone EUROIMAGE 1913076
355	332	AI087975	colon	metastatic	3	q28	Hs.195225	ESTs
356	409	AW001872	colon	metastatic	5	p13.1	Hs.58435	FYN binding protein (FYB-120/130)
357	408	M25753	colon	metastatic	5	q13.2	Hs.23960	cyclin B1
358	410	U70370	colon	metastatic	5	q31.1	Hs.84136	paired-like homeodomain transcription factor 1
359	434	AI739117	colon	metastatic	5	q31.2	Hs.73625	RAB6 interacting kinesin-like (rabkinesin6)
360	389	D14678	colon	metastatic	6	p21.32	Hs.20830	kinesin-like 2
361	427	AA059458	colon	metastatic	7	p14.1	Hs.28792	Homo sapiens cDNA FLJ11041 fis clone
362	436	AI343467	colon	metastatic	7	p14.1	Hs.28792	PLACE1004405
363	437	M13436	colon	metastatic	7	p14.1	Hs.727	Homo sapiens cDNA FLJ11041 fis clone
364	329	AK023208	colon	metastatic	7	p14.2	Hs.62180	PLACE1004405
365	438	AK023208	colon	metastatic	7	p14.2	Hs.62180	inhibin beta A (activin A activin AB alpha polypeptide)
366	440	AK023208	colon	metastatic	7	p14.2	Hs.62180	anillin actin binding protein (scraps homolog Drosophila)
								anillin actin binding protein (scraps homolog Drosophila)
								anillin actin binding protein (scraps homolog Drosophila)

Table 1 (Continued)

367	348	AI285531	colon	metastatic	7	p15.2	Hs.106260	Drosophila)
368	392	AI922323	colon	metastatic	7	p21.1	Hs.91011	sorting nexin 10
369	339	AI961907	colon	metastatic	7	q21.3	Hs.179573	anterior gradient 2 homolog (Xenopus laevis)
370	356	U61145	colon	metastatic	7	q36.1	Hs.77256	collagen type 1 alpha 2
371	336	AI949095	colon	metastatic	8	NULL	Hs.67776	enhancer of zeste homolog 2 (Drosophila)
372	362	AA625199	colon	metastatic	8	NULL	Hs.352415	Homo sapiens clone IMAGE:5455669 mRNA partial cds
373	439	AI932328	colon	metastatic	8	p21.1	Hs.104741	solute carrier family 39 (zinc transporter) member 4
374	428	AA203476	colon	metastatic	8	q13.2	Hs.252587	T-LAK cell-originated protein kinase
375	414	AW043713	colon	metastatic	8	q13.3	Hs.70823	pituitary tumor-transforming 1
376	345	AA524023	colon	metastatic	8	q21.13	Hs.2384	sulfatase FP
377	363	AF091433	colon	metastatic	8	q22.1	Hs.30464	tumor protein D52
378	342	AA610522	colon	metastatic	8	q24.11	Hs.162697	cyclin E2
379	373	AL117612	colon	metastatic	8	q24.12	Hs.76550	ESTs
380	347	D78130	colon	metastatic	8	q24.13	Hs.71465	mal T-cell differentiation protein 2
381	366	AI656807	colon	metastatic	8	q24.13	Hs.222088	squalene epoxidase
382	388	AA147884	colon	metastatic	8	q24.22	Hs.9812	hypothetical protein MGC5254
383	374	AV007586	colon	metastatic	9	q34.11	Hs.133122	Homo sapiens cDNA FLJ14388 fis clone HEMBA1002716
384	383	AI811865	colon	metastatic	9	q34.3	Hs.274152	zinc finger DHHC domain containing 12
385	393	W25552	colon	metastatic	9	q34.3	Hs.212613	EST
386	355	AF067656	colon	metastatic	10	q21.1	Hs.42650	hypothetical protein FLJ36779
387	368	X05360	colon	metastatic	10	q21.2	Hs.334562	ZW10 interactor
388	416	AI674163	colon	metastatic	10	q23.33	Hs.14559	cell division cycle 2 G1 to S and G2 to M
389	337	AA705015	colon	metastatic	11	p15.1	Hs.185918	hypothetical protein FLJ10540
390	372	AB018293	colon	metastatic	11	p15.3	Hs.314434	Homo sapiens cDNA FLJ32525 fis clone SMINT2000060
391	401	AL079372	colon	metastatic	11	q13.1	Hs.23044	KIAA0750 gene product
392	350	D60944	colon	metastatic	11	q13.4	Hs.84700	similar to RIKEN cDNA 2610036L13
393	379	AA704137	colon	metastatic	11	q23.3	Hs.125359	serologically defined colon cancer antigen 28
								Thy-1 cell surface antigen

Table 1 (Continued)

394	381	X14850	colon	metastatic	11	q23.3	Hs.147097	H2A histone family member X
395	429	U74612	colon	metastatic	12	p13.33	Hs.239	forkhead box M1
396	384	U82984	colon	metastatic	12	q13.12	Hs.23900	Rac GTPase activating protein 1
397	343	R61322	colon	metastatic	12	q24.31	Hs.204166	Human clone 295 5cM region surrounding hepatocyte nuclear factor-1a/MODY3 mRNA
398	353	AI291142	colon	metastatic	13	q33.3	Hs.183874	cullin 4A
399	387	L25876	colon	metastatic	14	q22.1	Hs.84113	cyclin-dependent kinase inhibitor 3 (CDK2-associated dual specificity phosphatase)
400	423	AL080146	colon	metastatic	15	q21.3	Hs.194698	cyclin B2
401	413	D14657	colon	metastatic	15	q22.2	Hs.81892	KIAA0101 gene product
402	406	AA195614	colon	metastatic	15	q25.3	Hs.344037	protein regulator of cytokinesis 1
403	407	BC003186	colon	metastatic	16	NULL	Hs.108196	HSPC037 protein
404	415	AW003626	colon	metastatic	16	NULL	Hs.159154	tubulin beta 4
405	358	AI701742	colon	metastatic	16	p13.3	Hs.290943	Homo sapiens similar to possible G-protein receptor clone MGC:21993 IMAGE:4398317 mRNA complete cds
406	361	BE965311	colon	metastatic	16	p13.3	Hs.124915	hypothetical protein MGC2601
407	364	AL520675	colon	metastatic	16	p13.3	Hs.351474	hypothetical protein FLJ30002
408	377	AI953838	colon	metastatic	16	p13.3	Hs.124015	hypothetical protein MGC2605
409	385	W92110	colon	metastatic	16	p13.3	Hs.279623	selenoprotein X 1
410	431	AI819340	colon	metastatic	16	p13.3	Hs.13561	hypothetical protein MGC4692
411	405	AA904482	colon	metastatic	16	q12.2	Hs.368078	ESTs
412	391	U81800	colon	metastatic	17	NULL	Hs.85838	solute carrier family 16 (monocarboxylic acid transporters) member 3
413	411	AI683036	colon	metastatic	17	NULL	Hs.314169	KIAA1618 protein
414	390	BE328850	colon	metastatic	17	q11.2	Hs.348504	hypothetical protein BC014072
415	376	L47276	colon	metastatic	17	q21.31	NULL	unknown
416	386	AI375913	colon	metastatic	17	q21.31	Hs.156346	topoisomerase (DNA) II alpha 170kDa
417	432	AW003286	colon	metastatic	17	q21.31	Hs.370428	ESTs Moderately similar to TP2A_HUMAN DNA topoisomerase II alpha isozyme [H.sapiens]
418	375	BC001038	colon	metastatic	17	q22	Hs.307036	Homo sapiens Similar to epsin 3 clone

Table 1 (Continued)

419	359	BF029215	colon	metastatic	17	q23.2	Hs.103512	MGC:1006 IMAGE:3505495 mRNA complete cds Homo sapiens cDNA FLJ36569 fis clone TRACH2010824 highly similar to Ribonucleoprotein
420	426	BG165011	colon	metastatic	17	q23.2	Hs.165909	ESTs Weakly similar to hypothetical protein FLJ20489 [Homo sapiens] [H.sapiens]
421	398	AI675178	colon	metastatic	17	q24.2	Hs.90207	hypothetical protein MGC11138
422	369	U28386	colon	metastatic	17	q24.3	Hs.159557	karyopherin alpha 2 (RAG cohort 1 importin alpha 1)
423	335	AI525822	colon	metastatic	17	q25.3	Hs.109706	hematological and neurological expressed 1
424	378	K02581	colon	metastatic	17	q25.3	Hs.105097	thymidine kinase 1 soluble
425	331	AF017790	colon	metastatic	18	p11.32	Hs.58169	highly expressed in cancer rich in leucine heptad repeats
426	404	AF017790	colon	metastatic	18	p11.32	Hs.58169	highly expressed in cancer rich in leucine heptad repeats
427	422	AA719022	colon	metastatic	19	q13.43	Hs.288549	ubiquitin UBF-fl
428	371	D80008	colon	metastatic	20	p11.21	Hs.36232	KIAA0186 gene product
429	399	AI990405	colon	metastatic	20	p11.23	Hs.194691	retinoic acid induced 3
430	402	AF098158	colon	metastatic	20	q11.1	Hs.9329	chromosome 20 open reading frame 1
431	370	AW003586	colon	metastatic	20	q11.22	Hs.274411	SCAN domain containing 1
432	433	U73379	colon	metastatic	20	q13.12	Hs.93002	ubiquitin-conjugating enzyme E2C
433	338	AA207074	colon	metastatic	20	q13.13	Hs.56237	breast carcinoma amplified sequence 4
434	430	AF041260	colon	metastatic	20	q13.2	Hs.129057	breast carcinoma amplified sequence 1
435	424	AF011468	colon	metastatic	20	q13.31	Hs.250822	serine/threonine kinase 6
436	435	AA535819	colon	metastatic	20	q13.32	Hs.83883	transmembrane prostate androgen induced RNA
437	394	X70940	colon	metastatic	20	q13.33	Hs.2642	eukaryotic translation elongation factor 1 alpha 2
438	367	AL035081	colon	metastatic	22	q13.1	Hs.250696	KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 3
439	397	Y15916	colon	metastatic	22	q13.1	Hs.172928	collagen type I alpha 1

Table 1 (Continued)

440	418	AI381686	colon	metastatic	22	q13.2	Hs.208912	hypothetical protein MGC861
441	506	AA905821	lung	primary	1	p31.3	Hs.145958	ESTs
442	508	AI056599	lung	primary	1	p31.3	Hs.120893	ESTs
443	511	AW070459	lung	primary	1	p31.3	Hs.259438	ESTs
444	527	AK022113	lung	primary	1	p31.3	Hs.301858	Homo sapiens cDNA FLJ13017 fis clone NT2RP3000628
445	528	AU151151	lung	primary	1	p31.3	Hs.11493	Homo sapiens cDNA FLJ13536 fis clone PLACE1006521
446	547	AB044807	lung	primary	1	p31.3	Hs.321197	PDZ domain protein (Drosophila inaD-like)
447	485	AA012917	lung	primary	1	p32.1	Hs.333541	beta-amyloid binding protein precursor
448	498	BF224444	lung	primary	1	p32.1	Hs.127274	ESTs
449	526	AU147177	lung	primary	1	p32.1	Hs.301237	Homo sapiens cDNA FLJ12095 fis clone HEMBB1002610
450	473	AA926959	lung	primary	1	q21.3	Hs.77550	p53-regulated DDA3
451	443	AI053741	lung	primary	1	q22	Hs.133294	ESTs
452	448	AI766666	lung	primary	1	q22	Hs.374850	apolipoprotein A-I binding protein
453	469	AI739071	lung	primary	1	q22	Hs.158515	hypothetical protein MGC13038
454	441	AF326731	lung	primary	1	q23.3	Hs.234545	cell division cycle associated 1
455	446	BC002906	lung	primary	1	q23.3	Hs.75939	uridine monophosphate kinase
456	442	AA182412	lung	primary	1	q25.3	Hs.32058	chromosome 1 open reading frame 19
457	482	AA725362	lung	primary	2	p11.1	NULL	unknown
458	472	AI990317	lung	primary	2	p13.1	Hs.154672	methylenetetrahydrofolate dehydrogenase (NAD+ dependent) methenyltetrahydrofolate cyclohydrolase
459	464	AI191897	lung	primary	2	p16.2	Hs.105223	Homo sapiens Similar to RIKEN cDNA 2510006C20 gene clone MGC:24001 IMAGE:4050858 mRNA complete cds
460	474	AI492879	lung	primary	2	p25.1	Hs.75319	ribonucleotide reductase M2 polypeptide
461	481	H24953	lung	primary	2	q13	NULL	unknown
462	451	AA749314	lung	primary	2	q31.1	Hs.333893	cell division cycle associated 7
463	519	C00851	lung	primary	5	p13.2	Hs.144264	ESTs Weakly similar to hypothetical protein FLJ20837 [Homo sapiens] [H.sapiens]

Table 1 (Continued)

464	458	AA383208	lung	primary	5	p15.1	Hs.125249	ESTs	
465	548	AA524353	lung	primary	6	p21.2	Hs.27693	peptidylprolyl isomerase (cyclophilin)-like 1	
466	522	AW005489	lung	primary	6	p21.31	Hs.139800	high mobility group AT-hook 1	
467	538	AI677701	lung	primary	6	p22.3	Hs.201619	hypothetical protein FLJ30829	
468	551	BG528420	lung	primary	6	p22.3	Hs.83484	SRY (sex determining region Y)-box 4	
469	467	AI439141	lung	primary	6	p23	Hs.261023	hypothetical protein FLJ20958	
470	539	AI279547	lung	primary	6	p24.1	Hs.8645	hypothetical protein LOC51256	
471	540	W27692	lung	primary	6	p24.2	Hs.273077	hypothetical protein MGC1223	
472	495	K03193	lung	primary	7	p11.2	Hs.77432	epidermal growth factor receptor	
								(erythroblastic leukemia viral (v-erb-b) oncogene homolog avian)	
473	496	AI806160	lung	primary	7	p11.2	Hs.127991	ESTs	
474	497	AW138673	lung	primary	7	p11.2	Hs.252928	ESTs	
475	502	H65306	lung	primary	7	p11.2	Hs.205559	ESTs	
476	509	AW971863	lung	primary	7	p11.2	Hs.103351	ESTs	
477	536	D60436	lung	primary	7	p11.2	Hs.335933	Homo sapiens clone MGC:33530	
478	545	AI363001	lung	primary	7	p11.2	Hs.134342	IMAGE:4820705 mRNA complete cds	
479	524	AV700815	lung	primary	7	p12.3	Hs.180171	LanC lantibiotic synthetase component C-like 2 (bacterial)	
480	486	AA740186	lung	primary	7	p13	Hs.81029	Homo sapiens cDNA FLJ10417 fis clone NT2RP1000112	
481	510	AI252004	lung	primary	7	p13	Hs.284148	biliverdin reductase A	
482	514	AW452419	lung	primary	7	p13	Hs.296098	ESTs	
483	515	AI418313	lung	primary	7	p13	Hs.152895	ESTs	
484	517	AI191118	lung	primary	7	p13	Hs.222015	ESTs Moderately similar to cytokine receptor-like factor 2 cytokine receptor CRL2 precursor [Homo sapiens]	
485	523	AI823792	lung	primary	7	p13	Hs.301005	histone H2A.F/Z variant	
486	533	AK025276	lung	primary	7	p13	Hs.306791	Homo sapiens cDNA: FLJ21623 fis clone COL07915	
487	534	AL137266	lung	primary	7	p13	Hs.332520	Homo sapiens mRNA cDNA DKFZp434A1014	



Table 1 (Continued)

488	542	BC004903	lung	primary	7	p13	Hs.9960	(from clone DKFZp434A1014) partial cds
489	546	AF192523	lung	primary	7	p13	Hs.47701	hypothetical protein MGC4607 NPC1 (Niemann-Pick disease type C1 gene)-like 1
490	550	AW194730	lung	primary	7	p13	Hs.9075	serine/threonine kinase 17a (apoptosis-inducing)
491	541	BC000769	lung	primary	7	p14.1	Hs.59594	hypothetical protein MGC2821
492	445	U97188	lung	primary	7	p15.3	Hs.79440	IGF-II mRNA-binding protein 3
493	465	AI910524	lung	primary	7	p15.3	Hs.87385	hypothetical protein BC012331
494	471	AI806483	lung	primary	7	p15.3	Hs.108931	membrane protein palmitoylated 6 (MAGUK p55 subfamily member 6)
495	494	AW402635	lung	primary	7	q22.1	Hs.375569	DNA directed RNA polymerase II polypeptide J-related gene
496	475	AI922792	lung	primary	8	NULL	Hs.239784	scribble
497	489	R51273	lung	primary	8	q12.2	Hs.250502	carbonic anhydrase VIII
498	500	BE465243	lung	primary	8	q13.2	Hs.12664	ESTs
499	503	AA132172	lung	primary	8	q13.2	Hs.19107	ESTs
500	549	AA203476	lung	primary	8	q13.2	Hs.252587	pituitary tumor-transforming 1
501	555	AF232217	lung	primary	8	q13.3	NULL	unknown
502	556	AF130055	lung	primary	8	q13.3	NULL	unknown
503	463	BF002104	lung	primary	8	q21.11	Hs.168950	Homo sapiens mRNA cDNA DKFZp566A1046 (from clone DKFZp566A1046)
504	507	AI335223	lung	primary	8	q21.11	Hs.133293	ESTs
505	512	AI370381	lung	primary	8	q21.11	Hs.128841	ESTs
506	529	AK024242	lung	primary	8	q21.11	Hs.296753	Homo sapiens cDNA FLJ14180 fis clone NT2RP2003799
507	530	AI701468	lung	primary	8	q21.11	Hs.60681	Homo sapiens cDNA FLJ34367 fis clone FEBRA2016621
508	480	BG389015	lung	primary	8	q21.13	Hs.2384	tumor protein D52
509	499	AA479492	lung	primary	8	q21.13	Hs.184387	ESTs
510	488	U07969	lung	primary	8	q22.1	Hs.89436	cadherin 17 LI cadherin (liver-intestine)
511	491	AF091433	lung	primary	8	q22.1	Hs.30464	cyclin E2

Table 1 (Continued)

512	490	AA584310	lung	primary	8	q22.3	Hs.283713	collagen triple helix repeat containing 1
513	505	AA904882	lung	primary	8	q22.3	Hs.130107	ESTs
514	543	AA451665	lung	primary	8	q24.13	Hs.222088	hypothetical protein MGC5254
515	493	W03103	lung	primary	8	q24.22	Hs.10669	development and differentiation enhancing factor 1
516	518	BF055351	lung	primary	8	q24.22	Hs.20247	ESTs Weakly similar to hypothetical protein FLJ20489 [Homo sapiens] [H.sapiens]
517	544	BF941325	lung	primary	8	q24.22	Hs.15611	KIAA1485 protein
518	535	AW137073	lung	primary	8	q24.23	Hs.176669	Homo sapiens mRNA cDNA DKFZp451M139 (from clone DKFZp451M139)
519	537	AA447947	lung	primary	12	p11.22	Hs.227591	hypothetical protein FLJ11088
520	456	R91766	lung	primary	12	p11.23	Hs.173074	DKFZP564O1863 protein
521	466	AF274950	lung	primary	12	p11.23	Hs.22595	hypothetical protein FLJ10637
522	470	AI334297	lung	primary	12	p11.23	Hs.51743	KIAA1340 protein
523	476	AW779556	lung	primary	12	p11.23	Hs.184523	serine/threonine kinase 38 like
524	478	AI688580	lung	primary	12	p11.23	Hs.286145	SRB7 suppressor of RNA polymerase B homolog (yeast)
525	483	AF161472	lung	primary	12	p11.23	NULL	unknown
526	504	BF724206	lung	primary	12	p11.23	Hs.221024	ESTs
527	525	AL118653	lung	primary	12	p11.23	Hs.284270	Homo sapiens cDNA FLJ11335 fis clone PLACE1010630
528	531	AI652982	lung	primary	12	p11.23	Hs.111583	Homo sapiens cDNA FLJ34764 fis clone NT2NE2002311
529	553	AA127950	lung	primary	12	p11.23	Hs.222024	transcription factor BMAL2
530	449	AI652662	lung	primary	12	p12.1	Hs.317432	branched chain aminotransferase 1 cytosolic
531	460	AU154905	lung	primary	12	p12.1	Hs.296734	Homo sapiens cDNA FLJ13318 fis clone OVARC1001600
532	461	AK025615	lung	primary	12	p12.1	Hs.7567	Homo sapiens cDNA: FLJ21962 fis clone HEP05564
533	462	AA829940	lung	primary	12	p12.1	Hs.301210	Homo sapiens mRNA cDNA DKFZp564F2072 (from clone DKFZp564F2072)
534	468	BE326710	lung	primary	12	p12.1	Hs.170994	hypothetical protein MGC10946

Table 1 (Continued)

535	484	AA015609	lung	primary	12	p12.1	Hs.351221	v-Ki-ras2 Kirsten rat sarcoma 2 viral oncogene homolog
536	501	W70242	lung	primary	12	p12.1	Hs.58086	ESTs
537	516	AI242023	lung	primary	12	p12.1	Hs.137003	ESTs
538	520	AI003792	lung	primary	12	p12.1	Hs.120439	ethanolamine kinase
539	554	AA669106	lung	primary	12	p12.2	Hs.108106	ubiquitin-like containing PHD and RING finger domains 1
540	459	BC003602	lung	primary	12	p12.3	Hs.36727	H2A histone family member J
541	487	AI392836	lung	primary	12	p13.31	Hs.12045	C2f protein
542	492	AI983033	lung	primary	12	p13.31	Hs.380623	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 11 (CHL 1-like helicase homolog S. cerevisiae)
543	521	U74612	lung	primary	12	p13.33	Hs.239	forkhead box M1
544	455	AF213033	lung	primary	14	q22.1	Hs.84113	cyclin-dependent kinase inhibitor 3 (CDK2-associated dual specificity phosphatase)
545	447	AF167438	lung	primary	14	q23.2	Hs.179817	androgen-regulated short-chain dehydrogenase/reductase 1
546	513	AI146765	lung	primary	18	p11.31	Hs.373550	ESTs
547	532	AW003207	lung	primary	18	p11.31	Hs.48659	Homo sapiens cDNA FLJ36057 fis clone TEST12018475 highly similar to LAMININ ALPHA-1 CHAIN PRECURSOR
548	444	AF017790	lung	primary	18	p11.32	Hs.58169	highly expressed in cancer rich in leucine heptad repeats
549	450	AB023169	lung	primary	20	p12.2	Hs.7935	BTB (POZ) domain containing 3
550	457	AI732446	lung	primary	20	p12.2	Hs.70903	ESTs
551	479	D21267	lung	primary	20	p12.2	Hs.84389	synaptosomal-associated protein 25kDa
552	452	Y00064	lung	primary	20	p12.3	Hs.2281	chromogranin B (secretogranin 1)
553	453	AI096882	lung	primary	20	p13	Hs.135056	chromosome 20 open reading frame 139
554	454	AI949781	lung	primary	20	p13	Hs.26802	chromosome 20 open reading frame 97
555	477	AI924533	lung	primary	20	p13	Hs.105607	solute carrier family 4 sodium bicarbonate transporter-like member 11
556	552	U85658	lung	primary	20	q13.31	Hs.61796	transcription factor AP-2 gamma (activating

Table 1 (Continued)

557	654	AW151887	lung	metastatic	1	p22.3	Hs.169939	enhancer binding protein 2 gamma)
558	651	BE645144	lung	metastatic	1	p31.1	Hs.374411	heparan sulfate 2-O-sulfotransferase 1
559	619	AI810054	lung	metastatic	1	p31.2	Hs.133260	ESTs Moderately similar to hypothetical protein FLJ20378 [Homo sapiens] [H.sapiens]
560	629	N32508	lung	metastatic	1	p31.2	Hs.8107	hypothetical protein FLJ20354
561	636	BC002488	lung	metastatic	1	p31.2	Hs.165998	G-protein gamma-12 subunit
562	628	AA618420	lung	metastatic	1	p32.1	Hs.299254	PAI-1 mRNA-binding protein
563	627	AW140098	lung	metastatic	1	p32.3	Hs.25821	Homo sapiens cDNA: FLJ23597 fis clone LNG15281
564	648	AW409848	lung	metastatic	1	p32.3	Hs.13036	Fas (TNFRSF6) associated factor 1
565	637	AF151063	lung	metastatic	1	p34.1	NULL	DKFZP727A071 protein
566	600	AA926959	lung	metastatic	1	q21.3	Hs.77550	unknown
567	576	AI766666	lung	metastatic	1	q22	Hs.374850	p53-regulated DDA3
568	588	AI690773	lung	metastatic	1	q22	Hs.133294	apolipoprotein A-I binding protein
569	601	AI739071	lung	metastatic	1	q22	Hs.158515	ESTs
570	561	AF326731	lung	metastatic	1	q23.3	Hs.234545	hypothetical protein MGC13038
571	562	D78335	lung	metastatic	1	q23.3	Hs.75939	cell division cycle associated 1
572	558	AA182412	lung	metastatic	1	q25.3	Hs.32058	uridine monophosphate kinase
573	599	AA725362	lung	metastatic	2	p11.1	NULL	chromosome 1 open reading frame 19
574	592	AI990317	lung	metastatic	2	p13.1	Hs.154672	unknown
575	603	AI191897	lung	metastatic	2	p16.2	Hs.105223	methylene tetrahydrofolate dehydrogenase (NAD+ dependent) methenyltetrahydrofolate cyclohydrolase
576	583	BC001886	lung	metastatic	2	p25.1	Hs.75319	Homo sapiens Similar to RIKEN cDNA 2510006C20 gene clone MGC:24001
577	605	H24953	lung	metastatic	2	q13	NULL	IMAGE:4050858 mRNA complete cds
578	575	AA749314	lung	metastatic	2	q31.1	Hs.333893	ribonucleotide reductase M2 polypeptide
579	579	AA868748	lung	metastatic	5	p15.1	Hs.125249	unknown
580	589	AI439141	lung	metastatic	6	p23	Hs.261023	cell division cycle associated 7
								ESTs
								hypothetical protein FLJ20958

Table 1 (Continued)

581	606	AU156822	lung	metastatic	7	p11.2	Hs.287577	Homo sapiens cDNA FLJ13503 fis clone PLACE1004838
582	607	U48722	lung	metastatic	7	p11.2	NULL	unknown
583	609	AA768884	lung	metastatic	7	p11.2	Hs.140489	Homo sapiens cDNA FLJ25559 fis clone JTH02834
584	610	AK000106	lung	metastatic	7	p11.2	Hs.272227	Homo sapiens cDNA FLJ20099 fis clone COL04544
585	613	AU147861	lung	metastatic	7	p11.2	Hs.188082	Homo sapiens cDNA FLJ12308 fis clone MAMMA1001931
586	616	BE737030	lung	metastatic	7	p11.2	Hs.82916	chaperonin containing TCP1 subunit 6A (zeta 1)
587	622	AW157070	lung	metastatic	7	p11.2	Hs.77432	epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog avian)
588	639	BE878463	lung	metastatic	7	p11.2	Hs.279898	Homo sapiens cDNA: FLJ23165 fis clone LNG09846
589	557	AK023208	lung	metastatic	7	p14.2	Hs.62180	anillin actin binding protein (scraps homolog Drosophila)
590	560	U97188	lung	metastatic	7	p15.3	Hs.79440	IGF-II mRNA-binding protein 3
591	577	AI910524	lung	metastatic	7	p15.3	Hs.87385	hypothetical protein BC012331
592	590	AI806483	lung	metastatic	7	p15.3	Hs.108931	membrane protein palmitoylated 6 (MAGUK p55 subfamily member 6)
593	617	AL136770	lung	metastatic	7	q21.13	Hs.258576	claudin 12
594	635	BF680588	lung	metastatic	7	q21.13	Hs.118258	Homo sapiens cDNA: FLJ23160 fis clone LNG09682
595	618	U19348	lung	metastatic	7	q31.2	NULL	unknown
596	638	BG170541	lung	metastatic	7	q31.2	Hs.285754	met proto-oncogene (hepatocyte growth factor receptor)
597	641	AI632244	lung	metastatic	7	q32.1	Hs.233694	putative methyltransferase
598	653	AI964022	lung	metastatic	7	q33	Hs.107394	secretory protein SEC8
599	593	AI922792	lung	metastatic	8	NULL	Hs.239784	scribble
600	644	AA723810	lung	metastatic	8	NULL	Hs.69517	cDNA for differentially expressed CO16 gene

Table 1 (Continued)

601	621	BF059124	lung	metastatic	8	q12.3	Hs.29419	ESTs
602	631	AA543030	lung	metastatic	8	q12.3	Hs.152409	ESTs
603	632	AF289489	lung	metastatic	8	q12.3	Hs.283664	aspartate beta-hydroxylase
604	646	AW663544	lung	metastatic	8	q13.1	Hs.85524	ring finger protein 29
605	581	BF002104	lung	metastatic	8	q21.11	Hs.168950	Homo sapiens mRNA cDNA DKFZp566A1046 (from clone DKFZp566A1046)
606	612	AI916600	lung	metastatic	8	q21.11	Hs.121194	Homo sapiens cDNA: FLJ21569 fis clone COL06508
607	623	AI625741	lung	metastatic	8	q21.11	Hs.21275	hypothetical protein FLJ11011
608	630	AW150720	lung	metastatic	8	q21.11	Hs.356086	ESTs Weakly similar to retinal short-chain dehydrogenase/reductase retSDR2 [Homo sapiens] [H.sapiens]
609	645	N89607	lung	metastatic	8	q21.11	Hs.184693	transcription elongation factor B (SIII)
610	650	W46994	lung	metastatic	8	q21.11	Hs.96870	polypeptide 1 (15kDa elongin C)
611	563	BG389015	lung	metastatic	8	q21.13	Hs.2384	staufen RNA binding protein homolog 2 (Drosophila)
612	633	AK000049	lung	metastatic	8	q21.13	Hs.183861	tumor protein D52
613	634	AK024296	lung	metastatic	8	q21.13	Hs.237146	hypothetical protein MGC22825
614	656	AL039862	lung	metastatic	8	q24.21	Hs.49136	zinc finger protein RINZF
615	611	M26095	lung	metastatic	11	p15.2	Hs.37058	Homo sapiens cDNA FLJ23705 fis clone HEP11066
616	565	AF256215	lung	metastatic	12	p11.23	Hs.222024	calcitonin/calcitonin-related polypeptide alpha transcription factor BMAL2
617	566	AI569851	lung	metastatic	12	p11.23	Hs.22595	hypothetical protein FLJ10637
618	573	AF161472	lung	metastatic	12	p11.23	NULL	unknown
619	574	U46837	lung	metastatic	12	p11.23	Hs.286145	SRB7 suppressor of RNA polymerase B homolog (yeast)
620	580	R91766	lung	metastatic	12	p11.23	Hs.173074	DKFZP564O1863 protein
621	584	AI334297	lung	metastatic	12	p11.23	Hs.51743	KIAA1340 protein
622	585	AW779556	lung	metastatic	12	p11.23	Hs.184523	serine/threonine kinase 38 like
623	586	BF540749	lung	metastatic	12	p11.23	Hs.111583	Homo sapiens cDNA FLJ34764 fis clone NT2NE2002311

Table 1 (Continued)

624	587	BC005176	lung	metastatic	12	p11.23	Hs.10071	seven transmembrane protein TM7SF3
625	564	AI652662	lung	metastatic	12	p12.1	Hs.317432	branched chain aminotransferase 1 cytosolic
626	568	AK025615	lung	metastatic	12	p12.1	Hs.7567	Homo sapiens cDNA: FLJ21962 fis clone HEP05564
627	570	BE326710	lung	metastatic	12	p12.1	Hs.170994	hypothetical protein MGC10946
628	595	AA829940	lung	metastatic	12	p12.1	Hs.301210	Homo sapiens mRNA cDNA DKFZp564F2072 (from clone DKFZp564F2072)
629	597	AA015609	lung	metastatic	12	p12.1	Hs.351221	v-Ki-ras2 Kirsten rat sarcoma 2 viral oncogene homolog
630	604	AU154905	lung	metastatic	12	p12.1	Hs.296734	Homo sapiens cDNA FLJ13318 fis clone OVARC1001600
631	571	AK025578	lung	metastatic	12	p12.2	Hs.108106	ubiquitin-like containing PHD and RING finger domains 1
632	578	BC003602	lung	metastatic	12	p12.3	Hs.36727	H2A histone family member J
633	643	AI743489	lung	metastatic	12	p13.1	Hs.322679	Homo sapiens cDNA FLJ36082 fis clone TEST12019998
634	642	AA102574	lung	metastatic	14	q12	Hs.8858	bromodomain adjacent to zinc finger domain 1A
635	620	AI953589	lung	metastatic	14	q13.1	Hs.146134	ESTs
636	608	AW268365	lung	metastatic	14	q21.3	Hs.25740	ERO1-like (S. cerevisiae)
637	626	BC006117	lung	metastatic	14	q21.3	Hs.222021	hypothetical protein FLJ12618
638	655	AJ292969	lung	metastatic	14	q21.3	Hs.288906	WW45 protein
639	567	AF213033	lung	metastatic	14	q22.1	Hs.84113	cyclin-dependent kinase inhibitor 3 (CDK2-associated dual specificity phosphatase)
640	652	BC005359	lung	metastatic	14	q22.1	Hs.151413	glia maturation factor beta
641	614	AI985034	lung	metastatic	14	q23.1	Hs.2704	glutathione peroxidase 2 (gastrointestinal)
642	624	AI554514	lung	metastatic	14	q23.1	Hs.97849	ESTs
643	569	AF167438	lung	metastatic	14	q23.2	Hs.179817	androgen-regulated short-chain dehydrogenase/reductase 1
644	625	AI654093	lung	metastatic	14	q23.2	Hs.43397	Homo sapiens cDNA FLJ37574 fis clone BRCOC2003100
645	647	BE465894	lung	metastatic	14	q24.2	Hs.98365	hypothetical protein FLJ39091

Table 1 (Continued)

646	615	AI969102	lung	metastatic	14	q32.11	Hs.172216	chromogranin A (parathyroid secretory protein 1)
647	640	AI656232	lung	metastatic	14	q32.11	Hs.90034	hypothetical protein FLJ21916
648	649	AI670847	lung	metastatic	14	q32.12	Hs.374662	Homo sapiens cDNA FLJ40513 fis clone TESTI2046456
649	559	AF017790	lung	metastatic	18	p11.32	Hs.58169	highly expressed in cancer rich in leucine heptad repeats
650	591	D21267	lung	metastatic	20	p12.2	Hs.84389	synaptosomal-associated protein 25kDa
651	598	AI732446	lung	metastatic	20	p12.2	Hs.70903	ESTs
652	602	AB023169	lung	metastatic	20	p12.2	Hs.7935	BTB (POZ) domain containing 3
653	572	Y00064	lung	metastatic	20	p12.3	Hs.2281	chromogranin B (secretogranin 1)
654	582	AI949781	lung	metastatic	20	p13	Hs.26802	chromosome 20 open reading frame 97
655	594	AF336127	lung	metastatic	20	p13	Hs.105607	solute carrier family 4 sodium bicarbonate transporter-like member 11
656	596	AI096882	lung	metastatic	20	p13	Hs.135056	chromosome 20 open reading frame 139
657	662	AK000490	prostate	primary	1	p31.2	Hs.133260	hypothetical protein FLJ20354
658	659	AW271106	prostate	primary	1	q22	Hs.133294	ESTs
659	660	AI053741	prostate	primary	1	q22	Hs.133294	ESTs
660	663	AA830844	prostate	primary	1	q23.2	Hs.127310	kinase interacting with leukemia-associated gene (statmin)
661	657	AF326731	prostate	primary	1	q23.3	Hs.234545	cell division cycle associated 1
662	661	AB032931	prostate	primary	1	q32.1	Hs.5199	HSPC150 protein similar to ubiquitin-conjugating enzyme
663	658	U30872	prostate	primary	1	q32.3	Hs.77204	centromere protein F 350/400ka (mitosin)
664	684	AI492879	prostate	primary	2	p25.1	Hs.75319	ribonucleotide reductase M2 polypeptide
665	683	N21131	prostate	primary	2	q37.3	Hs.42949	hairly and enhancer of split 6 (Drosophila)
666	690	BE407516	prostate	primary	5	q13.2	Hs.23960	cyclin B1
667	691	U70370	prostate	primary	5	q31.1	Hs.84136	paired-like homeodomain transcription factor 1
668	692	BE794699	prostate	primary	6	p21.2	Hs.284207	hypothetical protein BC003515
669	694	AI343467	prostate	primary	7	p14.1	Hs.28792	Homo sapiens cDNA FLJ11041 fis clone PLACE1004405
670	695	M13436	prostate	primary	7	p14.1	Hs.727	inhibin beta A (activin A activin AB alpha



Table 1 (Continued)

671	693	AK023208	prostate	primary	7	p14.2	Hs.62180	polypeptide) anillin actin binding protein (scraps homolog Drosophila)
672	698	AI932328	prostate	primary	8	p21.1	Hs.104741	T-LAK cell-originated protein kinase
673	697	AA203476	prostate	primary	8	q13.2	Hs.252587	pituitary tumor-transforming 1
674	696	AI925583	prostate	primary	8	q24.13	Hs.222088	hypothetical protein MGC5254
675	700	BE544837	prostate	primary	9	q33.2	Hs.352417	Homo sapiens Similar to RIKEN cDNA 3321402G02 gene clone MGC:23929 IMAGE:4807540 mRNA complete cds
676	699	AI983261	prostate	primary	9	q34.3	Hs.323445	ESTs Weakly similar to T2D3_HUMAN Transcription initiation factor TFIIID 135 kDa subunit (TAFII-135) (TAFII135)
677	664	X05360	prostate	primary	10	q21.2	Hs.334562	cell division cycle 2 G1 to S and G2 to M
678	665	AI674163	prostate	primary	10	q23.33	Hs.14559	hypothetical protein FLJ10540
679	666	BE614410	prostate	primary	11	q13.1	Hs.23044	similar to RIKEN cDNA 2610036L13
680	667	U74612	prostate	primary	12	p13.33	Hs.239	forkhead box M1
681	668	R61322	prostate	primary	12	q24.31	Hs.204166	Human clone 295 5cM region surrounding hepatocyte nuclear factor-1a/MODY3 mRNA
682	669	L25876	prostate	primary	14	q22.1	Hs.84113	cyclin-dependent kinase inhibitor 3 (CDK2- associated dual specificity phosphatase)
683	670	U65410	prostate	primary	14	q23.1	Hs.79078	MAD2 mitotic arrest deficient-like 1 (yeast)
684	671	AL080146	prostate	primary	15	q21.3	Hs.194698	cyclin B2
685	672	D14657	prostate	primary	15	q22.2	Hs.81892	KIAA0101 gene product
686	674	AB018009	prostate	primary	16	NULL	Hs.184601	solute carrier family 7 (cationic amino acid transporter y+ system) member 5
687	673	AI819340	prostate	primary	16	p13.3	Hs.13561	hypothetical protein MGC4692
688	678	BE328850	prostate	primary	17	q11.2	Hs.348504	hypothetical protein BC014072
689	679	AF063308	prostate	primary	17	q11.2	Hs.16244	mitotic spindle coiled-coil related protein
690	676	AW003286	prostate	primary	17	q21.31	Hs.370428	ESTs Moderately similar to TP2A_HUMAN DNA topoisomerase II alpha isozyme [H.sapiens]
691	680	AI375913	prostate	primary	17	q21.31	Hs.156346	topoisomerase (DNA) II alpha 170kDa

Table 1 (Continued)

692	681	L47276	prostate	primary	17	q21.31	NULL	unknown
693	677	BG165011	prostate	primary	17	q23.2	Hs.165909	ESTs Weakly similar to hypothetical protein FLJ20489 [Homo sapiens] [H.sapiens]
694	675	BF056791	prostate	primary	17	q23.3	Hs.87507	ESTs
695	682	AA719022	prostate	primary	19	q13.43	Hs.288549	ubiquitin UBF-f1
696	686	D80008	prostate	primary	20	p11.21	Hs.36232	KIAA0186 gene product
697	685	AF098158	prostate	primary	20	q11.1	Hs.9329	chromosome 20 open reading frame 1
698	688	U73379	prostate	primary	20	q13.12	Hs.93002	ubiquitin-conjugating enzyme E2C
699	687	AF011468	prostate	primary	20	q13.31	Hs.250822	serine/threonine kinase 6
700	701	T77624	prostate	primary	21	q22.13	Hs.79375	holocarboxylase synthetase (biotin-[propionyl-Coenzyme A-carboxylase (ATP-hydrolysing)] ligase)
701	689	AI381686	prostate	primary	22	q13.2	Hs.208912	hypothetical protein MGC861
702	723	AA630330	prostate	metastatic	1	q21.2	Hs.89545	proteasome (prosome macropain) subunit beta type 4
703	771	AW271106	prostate	metastatic	1	q22	Hs.133294	ESTs
704	773	AI690773	prostate	metastatic	1	q22	Hs.133294	ESTs
705	803	AI766666	prostate	metastatic	1	q22	Hs.374850	apolipoprotein A-I binding protein
706	739	AI249980	prostate	metastatic	1	q23.2	Hs.127310	kinase interacting with leukemia-associated gene (stathmin)
707	798	AI015982	prostate	metastatic	1	q23.3	Hs.234545	cell division cycle associated 1
708	745	H62656	prostate	metastatic	1	q24.3	Hs.300893	hypothetical protein MGC17528
709	753	N29457	prostate	metastatic	1	q31.1	Hs.117305	hypothetical gene supported by BC007071
710	796	U30872	prostate	metastatic	1	q32.3	Hs.77204	centromere protein F 350/400ka (mitotin)
711	794	AA151971	prostate	metastatic	1	q42.2	Hs.334372	chorionic somatomammotropin hormone 2
712	748	AI971357	prostate	metastatic	3	p21.32	Hs.146170	hypothetical protein FLJ22969
713	778	W24316	prostate	metastatic	3	q12.3	Hs.173374	endothelial and smooth muscle cell-derived neuropilin-like protein
714	716	AI338462	prostate	metastatic	3	q26.1	Hs.50758	SMC4 structural maintenance of chromosomes 4-like 1 (yeast)
715	717	AB019987	prostate	metastatic	3	q26.1	Hs.50758	SMC4 structural maintenance of chromosomes 4-like 1 (yeast)

Table 1 (Continued)

716	740	AL119157	prostate	metastatic	3	q26.32	Hs.22941	KIAA1363 protein
717	777	BG170335	prostate	metastatic	3	q26.32	Hs.122579	epithelial cell transforming sequence 2
718	704	AI968388	prostate	metastatic	3	q26.33	NULL	oncogene
719	724	AA194529	prostate	metastatic	3	q28	Hs.74619	unknown
720	760	BE256479	prostate	metastatic	5	p14.3	Hs.79037	proteasome (prosome macropain) 26S subunit
721	705	AI750154	prostate	metastatic	5	p15.1	NULL	non-ATPase 2
722	711	U96131	prostate	metastatic	5	p15.33	Hs.6566	heat shock 60kDa protein 1 (chaperonin)
723	787	M25753	prostate	metastatic	5	q13.2	Hs.23960	unknown
724	758	AI369840	prostate	metastatic	6	p21.1	Hs.374582	thyroid hormone receptor interactor 13
725	804	AK023208	prostate	metastatic	7	p14.2	Hs.62180	cyclin B1
726	752	AI910524	prostate	metastatic	7	p15.3	Hs.87385	Homo sapiens cDNA FLJ11842 fis clone
727	721	L07493	prostate	metastatic	7	p21.3	Hs.1608	HEMBA1006652 weakly similar to 60S
728	730	AL582836	prostate	metastatic	7	q21.3	Hs.137476	RIBOSOMAL PROTEIN L7
729	770	AI922470	prostate	metastatic	7	q21.3	Hs.370106	anillin actin binding protein (scraps homolog
730	726	L37127	prostate	metastatic	7	q22.1	Hs.80475	Drosophila)
731	736	AA193396	prostate	metastatic	7	q31.2	Hs.285754	hypothetical protein BC012331
732	768	AI679933	prostate	metastatic	7	q33	Hs.369347	replication protein A3 14kDa
733	763	AI571298	prostate	metastatic	8	NULL	Hs.343589	paternally expressed 10
734	732	AA191576	prostate	metastatic	8	q12.1	Hs.9614	ESTs Highly similar to asparagine synthetase
735	801	AW001796	prostate	metastatic	8	q12.3	Hs.283664	[Homo sapiens] [H.sapiens]
736	729	AA203476	prostate	metastatic	8	q13.2	Hs.252587	polymerase (RNA) II (DNA directed)
737	795	AI525903	prostate	metastatic	8	q13.3	Hs.118554	polypeptide J 13.3kDa
								met proto-oncogene (hepatocyte growth factor
								receptor)
								ESTs Weakly similar to hypothetical protein
								FLJ20378 [Homo sapiens] [H.sapiens]
								exosome component Rrp41
								nucleophosmin (nucleolar phosphoprotein B23
								numatrin)
								aspartate beta-hydroxylase
								pituitary tumor-transforming 1
								CGI-83 protein

Table 1 (Continued)

738	710	AA995715	prostate	metastatic	8	q21.11	Hs.184693	transcription elongation factor B (SIII) polypeptide 1 (15kDa elongin C)
739	782	BE409290	prostate	metastatic	8	q22.3	Hs.273344	DKFZP564O0463 protein
740	788	AA584310	prostate	metastatic	8	q22.3	Hs.283713	collagen triple helix repeat containing 1
741	769	BF109660	prostate	metastatic	8	q23.1	Hs.127286	ESTs Moderately similar to leucine-rich neuronal protein [Homo sapiens] [H.sapiens]
742	789	AI802955	prostate	metastatic	8	q23.2	Hs.195870	chronic myelogenous leukemia tumor antigen 66
743	737	AL117612	prostate	metastatic	8	q24.12	Hs.76550	mal T-cell differentiation protein 2
744	756	AI880004	prostate	metastatic	8	q24.22	Hs.356036	Homo sapiens mRNA cDNA DKFZp666E036 (from clone DKFZp666E036)
745	784	AI023398	prostate	metastatic	8	q24.22	Hs.10669	development and differentiation enhancing factor 1
746	706	AA527374	prostate	metastatic	8	q24.23	NULL	unknown
747	702	AF067656	prostate	metastatic	10	q21.1	Hs.42650	ZW10 interactor
748	799	AF154332	prostate	metastatic	10	q21.2	Hs.334562	cell division cycle 2 G1 to S and G2 to M
749	802	BC006121	prostate	metastatic	10	q22.1	Hs.117062	apoptosis-inducing factor (AIF)-homologous mitochondrion-associated inducer of death
750	728	K03226	prostate	metastatic	10	q22.2	Hs.77274	plasminogen activator urokinase
751	805	U90339	prostate	metastatic	10	q22.2	Hs.94382	adenosine kinase
752	725	AI198535	prostate	metastatic	10	q22.3	Hs.89463	potassium large conductance calcium-activated channel subfamily M alpha member 1
753	734	N27428	prostate	metastatic	10	q23.31	Hs.240	M-phase phosphoprotein 1
754	751	AI674163	prostate	metastatic	10	q23.33	Hs.14559	hypothetical protein FLJ10540
755	718	BE614410	prostate	metastatic	11	q13.1	Hs.23044	similar to RIKEN cDNA 2610036L13
756	761	BG251266	prostate	metastatic	11	q13.1	Hs.283565	FOS-like antigen 1
757	733	AA621983	prostate	metastatic	11	q13.3	Hs.116051	myeloma overexpressed gene (in a subset of t(11 14) positive multiple myelomas)
758	722	U82984	prostate	metastatic	12	q13.12	Hs.23900	Rac GTPase activating protein 1
759	747	AF091087	prostate	metastatic	12	q13.12	Hs.206501	hypothetical protein from clone 643
760	754	AI936946	prostate	metastatic	12	q13.12	Hs.121973	Homo sapiens clone MGC:20874

Table 1 (Continued)

761	707	AL118633	prostate	metastatic	12	q13.13	Hs.151678	IMAGE:4547239 mRNA complete cds
762	741	X81420	prostate	metastatic	12	q13.13	Hs.32952	UDP-N-acetyl-alpha-D-
763	762	D79987	prostate	metastatic	12	q13.13	Hs.153479	galactosamine:polypeptide N-
764	727	AF025840	prostate	metastatic	14	q21.2	Hs.99185	acetyl/galactosaminyltransferase 6 (GalNAc-T6)
765	744	AA648933	prostate	metastatic	14	q21.2	Hs.374811	keratin hair basic 1
766	749	BC006117	prostate	metastatic	14	q21.3	Hs.222021	extra spindle poles like 1 (S. cerevisiae)
767	750	AI924794	prostate	metastatic	14	q21.3	Hs.27931	polymerase (DNA directed) epsilon 2 (p59 subunit)
768	776	AW268365	prostate	metastatic	14	q21.3	Hs.25740	hypothetical protein MGC20689
769	780	D13633	prostate	metastatic	14	q22.1	Hs.77695	hypothetical protein FLJ12618
770	785	L25876	prostate	metastatic	14	q22.1	Hs.84113	hypothetical protein FLJ10607 similar to glucosamine-phosphate N-acetyltransferase ERO1-like (S. cerevisiae)
771	766	AI417084	prostate	metastatic	14	q22.2	Hs.301231	Drosophila discs large-1 tumor suppressor-like cyclin-dependent kinase inhibitor 3 (CDK2-associated dual specificity phosphatase) ESTs Weakly similar to PSA3_HUMAN Proteasome subunit alpha type 3 (Proteasome component C8) (Macropain)
772	735	J04031	prostate	metastatic	14	q23.1	Hs.172665	methylentetrahydrofolate dehydrogenase (NADP+ dependent) methenyltetrahydrofolate cyclohydrolase formyltetrahydrofolate synthetase
773	738	U65410	prostate	metastatic	14	q23.1	Hs.79078	MAD2 mitotic arrest deficient-like 1 (yeast)
774	731	AA926959	prostate	metastatic	14	q32.12	Hs.77550	p53-regulated DDA3
775	764	AL080102	prostate	metastatic	14	q32.2	Hs.334810	eukaryotic translation initiation factor 5
776	779	BF000332	prostate	metastatic	14	q32.2	Hs.7720	dynein cytoplasmic heavy polypeptide 1
777	786	AI525727	prostate	metastatic	14	q32.2	Hs.38205	cyclin-dependent kinase 2-interacting protein
778	800	AI761729	prostate	metastatic	14	q32.2	Hs.12908	CDC42 binding protein kinase beta (DMPK-like)
779	746	T65554	prostate	metastatic	14	q32.31	Hs.317821	hypothetical protein MGC13251

Table 1 (Continued)

780	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens clone MGC:16771 IMAGE:3907551 mRNA complete cds
781	797	A1684508	prostate	metastatic	14	q32.31	Hs.34045	cell division cycle associated 4
782	715	U81800	prostate	metastatic	17	NULL	Hs.85838	solute carrier family 16 (monocarboxylic acid transporters) member 3
783	774	A1292123	prostate	metastatic	17	NULL	Hs.201390	ESTs
784	743	A1458014	prostate	metastatic	17	q22	Hs.283558	hypothetical protein PRO1855
785	775	AA564822	prostate	metastatic	17	q22	Hs.298564	ESTs
786	767	BG165011	prostate	metastatic	17	q23.2	Hs.165909	ESTs Weakly similar to hypothetical protein FLJ20489 [Homo sapiens] [H.sapiens]
787	742	U28386	prostate	metastatic	17	q24.3	Hs.159557	karyopherin alpha 2 (RAG cohort 1 importin alpha 1)
788	713	K02581	prostate	metastatic	17	q25.3	Hs.105097	thymidine kinase 1 soluble
789	719	AA312511	prostate	metastatic	17	q25.3	Hs.273307	signal recognition particle 68kDa
790	759	A1525822	prostate	metastatic	17	q25.3	Hs.109706	hematological and neurological expressed 1
791	772	A1733461	prostate	metastatic	18	p11.22	Hs.127716	ESTs
792	783	AB000277	prostate	metastatic	18	p11.31	Hs.75814	discs large (Drosophila) homolog-associated protein 1
793	712	X02308	prostate	metastatic	18	p11.32	Hs.82962	thymidylate synthetase
794	709	M91670	prostate	metastatic	19	q13.42	Hs.174070	ubiquitin carrier protein
795	708	AA719022	prostate	metastatic	19	q13.43	Hs.288549	ubiquitin UBF-fl
796	792	A1761506	prostate	metastatic	20	p13	Hs.274422	chromosome 20 open reading frame 27
797	793	H06350	prostate	metastatic	20	p13	Hs.135056	chromosome 20 open reading frame 139
798	720	AF011468	prostate	metastatic	20	q13.31	Hs.250822	serine/threonine kinase 6
799	714	AW016409	prostate	metastatic	20	q13.33	Hs.235782	solute carrier family 21 (organic anion transporter) member 12
800	765	X70940	prostate	metastatic	20	q13.33	Hs.2642	eukaryotic translation elongation factor 1 alpha 2
801	791	A1652030	prostate	metastatic	21	q22.11	Hs.49932	chromosome 21 open reading frame 45
802	703	A1861913	prostate	metastatic	21	q22.3	Hs.143638	WD repeat domain 4
803	757	AA577678	prostate	metastatic	21	q22.3	Hs.282961	Homo sapiens cDNA FLJ35467 fis clone SMINT2005624

Table 1 (Continued)

804	781	AI860822	prostate	metastatic	21	q22.3	Hs.110757	DNA segment on chromosome 21 (unique) 2056 expressed sequence	
805	790	AI983544	prostate	metastatic	21	q22.3	Hs.126522	chromosome 21 open reading frame 70	Protein
806	120	R62346	breast	metastatic	1	q23.2	NULL	unknown	Protein
807	120	R62346	breast	metastatic	1	q23.2	NULL	unknown	Protein
808	120	R62346	breast	metastatic	1	q23.2	NULL	unknown	Protein
809	120	R62346	breast	metastatic	1	q23.2	NULL	unknown	Protein
810	120	R62346	breast	metastatic	1	q23.2	NULL	unknown	Protein
811	120	R62346	breast	metastatic	1	q23.2	NULL	unknown	Transcript
812	120	R62346	breast	metastatic	1	q23.2	NULL	unknown	Transcript
813	120	R62346	breast	metastatic	1	q23.2	NULL	unknown	Transcript
814	120	R62346	breast	metastatic	1	q23.2	NULL	unknown	Transcript
815	120	R62346	breast	metastatic	1	q23.2	NULL	unknown	Transcript
816	120	R62346	breast	metastatic	1	q23.2	NULL	unknown	Transcript
817	120	R62346	breast	metastatic	1	q23.2	NULL	unknown	Transcript
818	197	AA663786	breast	metastatic	3	p21.31	NULL	unknown	Transcript
819	194	AI962335	breast	metastatic	3	p24.3	Hs.196042	ESTs	Transcript
820	227	W25552	breast	metastatic	9	q34.3	Hs.212613	hypothetical protein FLJ36779	Protein
821	227	W25552	breast	metastatic	9	q34.3	Hs.212613	hypothetical protein FLJ36779	Transcript
822	77	AI962335	breast	primary	3	p24.3	Hs.196042	ESTs	Transcript
823	101	W25552	breast	primary	9	q34.3	Hs.212613	hypothetical protein FLJ36779	Protein
824	101	W25552	breast	primary	9	q34.3	Hs.212613	hypothetical protein FLJ36779	Transcript
825	334	AI962335	colon	metastatic	3	p24.3	Hs.196042	ESTs	Transcript
826	393	W25552	colon	metastatic	9	q34.3	Hs.212613	hypothetical protein FLJ36779	Protein
827	393	W25552	colon	metastatic	9	q34.3	Hs.212613	hypothetical protein FLJ36779	Transcript
828	301	AI962335	colon	primary	3	p24.3	Hs.196042	ESTs	Transcript
829	328	W25552	colon	primary	9	q34.3	Hs.212613	hypothetical protein FLJ36779	Protein
830	328	W25552	colon	primary	9	q34.3	Hs.212613	hypothetical protein FLJ36779	Transcript
831	527	AK022113	lung	primary	1	p31.3	Hs.301858	Homo sapiens cDNA FLJ13017 fis, clone NT2RP3000628	Transcript
832	527	AK022113	lung	primary	1	p31.3	Hs.301858	Homo sapiens cDNA FLJ13017 fis, clone NT2RP3000628	Transcript

Table 1 (Continued)

833	458	AA383208	lung	primary	5	p15.1	Hs.125249	ESTs	Protein
834	458	AA383208	lung	primary	5	p15.1	Hs.125249	ESTs	Transcript
835	519	C00851	lung	primary	5	p13.2	Hs.144264	ESTs, Weakly similar to hypothetical protein FLJ20837 [Homo sapiens]	Transcript
836	505	AA904882	lung	primary	8	q22.3	Hs.130107	[H.sapiens]	Transcript
837	529	AK024242	lung	primary	8	q21.11	Hs.296753	ESTs	Transcript
838	529	AK024242	lung	primary	8	q21.11	Hs.296753	Homo sapiens cDNA FLJ14180 fis, clone NT2RP2003799	Protein
839	555	AF232217	lung	primary	8	q13.3	NULL	Homo sapiens cDNA FLJ14180 fis, clone NT2RP2003799	Protein
840	513	AI146765	lung	primary	18	p11.31	Hs.373550	unknown	Transcript
841	753	N29457	prostate	metastatic	1	q31.1	Hs.117305	ESTs	Transcript
842	753	N29457	prostate	metastatic	1	q31.1	Hs.117305	hypothetical gene supported by BC007071	Protein
843	753	N29457	prostate	metastatic	1	q31.1	Hs.117305	hypothetical gene supported by BC007071	Protein
844	753	N29457	prostate	metastatic	1	q31.1	Hs.117305	hypothetical gene supported by BC007071	Protein
845	753	N29457	prostate	metastatic	1	q31.1	Hs.117305	hypothetical gene supported by BC007071	Protein
846	753	N29457	prostate	metastatic	1	q31.1	Hs.117305	hypothetical gene supported by BC007071	Transcript
847	753	N29457	prostate	metastatic	1	q31.1	Hs.117305	hypothetical gene supported by BC007071	Transcript
848	753	N29457	prostate	metastatic	1	q31.1	Hs.117305	hypothetical gene supported by BC007071	Protein
849	753	N29457	prostate	metastatic	1	q31.1	Hs.117305	hypothetical gene supported by BC007071	Transcript
850	753	N29457	prostate	metastatic	1	q31.1	Hs.117305	hypothetical gene supported by BC007071	Transcript



Table 1 (Continued)

851	753	N29457	prostate	metastatic	1	q31.1	Hs.117305	hypothetical gene supported by BC007071	Transcript
852	753	N29457	prostate	metastatic	1	q31.1	Hs.117305	hypothetical gene supported by BC007071	Transcript
853	753	N29457	prostate	metastatic	1	q31.1	Hs.117305	hypothetical gene supported by BC007071	Transcript
854	753	N29457	prostate	metastatic	1	q31.1	Hs.117305	hypothetical gene supported by BC007071	Transcript
855	705	AI750154	prostate	metastatic	5	p15.1	NULL	unknown	Protein
856	705	AI750154	prostate	metastatic	5	p15.1	NULL	unknown	Transcript
857	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
858	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
859	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
860	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein0
861	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
862	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
863	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
864	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
865	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
866	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
867	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein

Table 1 (Continued)

868	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
869	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
870	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
871	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein0
872	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
873	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
874	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
875	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
876	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
877	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
878	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
879	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
880	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
881	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
882	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
883	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein

Table 1 (Continued)

884	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
885	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
886	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
887	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
888	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
889	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Protein
890	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
891	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
892	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
893	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
894	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
895	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
896	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
897	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
898	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
899	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript

Table 1 (Continued)

900	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
901	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
902	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
903	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
904	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
905	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
906	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
907	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
908	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
909	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
910	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
911	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
912	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
913	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
914	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
915	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript

Table 1 (Continued)

916	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
917	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
918	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
919	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
920	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
921	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
922	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript
923	755	H04885	prostate	metastatic	14	q32.31	Hs.72363	Homo sapiens, clone MGC:16771 IMAGE:3907551, mRNA, complete cds	Transcript

WHAT IS CLAIMED IS:

1. A method for diagnosing cancer in a mammal, comprising  
determining amplification of a gene in the genome of a mammal wherein said  
5 gene is a gene of Table 1.

2. The method of claim 1 wherein said cancer is a member selected  
from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian  
cancer, pancreatic cancer, cervical cancer and kidney cancer.

10

3. The method of claim 1 wherein said gene of Table 1 is a gene that  
encodes the same gene product as a polynucleotide selected from the  
polynucleotides of SEQ ID NO: 1 – 805 and 855 - 923.

15

4. The method of claim 1 wherein said mammal is a human patient.

5. A method for diagnosing cancer or a pre-cancerous condition in a  
mammal, comprising:

(a) obtaining a cell or tissue sample from a mammal suspected of  
20 having cancer or a pre-cancerous condition and determining for said sample  
the gene copy number of a gene of Table 1;

(b) comparing said gene copy number of step (a) to the gene copy  
number of the same gene from a sample of a corresponding cell or tissue  
from a mammal of the same species not having cancer of the type being  
25 diagnosed

whereby a higher gene copy number determined in step (a) relative  
to that in step (b) indicates the presence of a cancer or pre-cancerous  
condition in the mammal of step (a) and results in a diagnosis of cancer or a  
pre-cancerous condition in said mammal.

30

6. The method of claim 5 wherein said mammal is a human patient.

7. The method of claim 5 wherein said cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

5           8. The method of claim 5 wherein the gene of Table 1 is a gene that encodes the same gene product as a polynucleotide of SEQ ID NO: 1 – 805 and 855– 923.

9. A method of inhibiting cancer, or a pre-cancerous condition, in a  
10 mammalian cell, comprising contacting said cell with a molecule that inhibits function of a gene of Table 1.

10. The method of claim 9 wherein said gene of Table 1 is a gene that encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805  
15 and 855 - 923.

11. The method of claim 9 wherein said molecule inhibits gene function by binding to said gene.

20           12. The method of claim 9 wherein said molecule inhibits gene function by binding to an RNA encoded by said gene.

13. The method of claim 9 wherein said molecule inhibits gene function by binding to polypeptide encoded by said gene.

25

14. The method of claim 9 wherein said molecule is a member selected from an antisense DNA, an antisense RNA, a ribozyme and an siRNA.

15. The method of claim 9 wherein said cancer is a member selected  
30 from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

16. The method of claim 9 wherein said contacting occurs in vivo.

17. A method for identifying an agent having therapeutic activity in a human patient in need of said therapeutic activity, comprising:

5 (a) determining in a sample from a patient the level of a gene product encoded by a gene of Table 1 prior to administering a test compound to said patient;

(b) administering said test compound to said patient;

(c) determining in a sample from said patient the level of a gene product encoded by the same the gene as in step (a)

10 wherein a decrease in the level of said gene product in step (c) relative to step (a) identifies said test compound as an agent having therapeutic activity.

18. The method of claim 17 wherein said therapeutic activity is  
15 anticancer activity.

19. The method of claim 17 wherein said cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

20

20. The method of claim 17 wherein said gene product is an RNA.

21. The method of claim 17 wherein said gene product is a polypeptide.

25

22. The method of claim 21 wherein said determination of said polypeptide is a determination of an enzyme activity.

23. The method of claim 17 wherein said gene of Table 1 is a gene that  
30 encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923.



24. The method of claim 17 wherein said molecule is a member selected from an antisense DNA, an antisense RNA, a ribozyme and an siRNA.

- 5           25. A method for identifying an antineoplastic agent, comprising:  
          (a) contacting a test compound with a cell that expresses a gene of  
Table 1; and  
          (b) determining a change in gene expression as a result of said  
contacting;  
10           whereby said change in said gene expression identifies said test  
compound as an antineoplastic agent.

26. The method of claim 25 wherein said change in expression is a decrease in expression.

- 15           27. The method of claim 25 wherein said contacting occurs in vivo.

28. The method of claim 25 wherein said gene of Table 1 encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923.

- 20           29. The method of claim 25 wherein said molecule is a member selected from an antisense DNA, an antisense RNA, ribozyme, an siRNA, a small organic molecule and an antibody.

- 25           30. A method for determining the cancerous status of a cell, comprising determining elevated expression in said cell of a gene of Table 1 wherein elevated expression of said gene indicates that said cell is cancerous.

31. The method of claim 30 wherein said elevated expression is an  
30   elevated copy number of the gene.

32. The method of claim 30 wherein said gene of Table 1 encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923.

33. A method for identifying a compound as an anti-neoplastic agent,  
5 comprising:

(a) contacting a test compound with a polypeptide encoded by a gene of Table 1,

(b) determining a change in a biological activity of said polypeptide due to said contacting,

10 wherein a change in activity identifies said test compound as an agent having antineoplastic activity.

34. The method of claim 33 wherein said gene of Table encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923.  
15

35. The method of claim 33 wherein said change in biological activity is a decrease in biological activity.

36. The method of claim 33 wherein said biological activity is an  
20 enzyme activity.

37. The method of claim 36 wherein said enzyme is selected from kinase, protease, peptidase, phosphodiesterase, phosphatase, dehydrogenase, reductase, carboxylase, transferase, deacetylase and  
25 polymerase.

38. The method of claim 37 wherein said kinase is a protein kinase.

39. The method of claim 37 wherein said kinase is a serine or  
30 threonine kinase.

40. The method of claim 37 wherein said kinase is a receptor tyrosine protein kinase.

41. The method of claim 37 wherein said protease is a serine protease,  
5 cysteine protease or aspartic acid protease.

42. The method of claim 37 wherein said transferase is a methyltransferase.

10 43. The method of claim 42 wherein said methyl transferase is a cytidine methyltransferase or an adenine methyltransferase.

44. The method of claim 37 wherein said deacetylase is a histone deacetylase.

15 45. The method of claim 37 wherein said carboxylase is a  $\gamma$ -carboxylase.

46. The method of claim 37 wherein said peptidase is a zinc peptidase.  
20

47. The method of claim 37 wherein said polymerase is a DNA polymerase.

48. The method of claim 37 wherein said polymerase is a RNA  
25 polymerase.

49. The method of claim 33 wherein said biological activity is a membrane transport activity.

30 50. The method of claim 33 wherein said polypeptide is a cation channel protein, an anion channel protein, a gated-ion channel protein or an ABC transporter protein.

51. The method of claim 33 wherein said polypeptide is an integrin.

52. The method of claim 33 wherein said polypeptide is a Cytochrome P450 enzyme.

5

53. The method of claim 33 wherein said polypeptide is a nuclear hormone receptor.

54. The method of claim 33 wherein said biological activity is a receptor activity.

10

55. The method of claim 33 wherein said receptor is a G-protein-coupled receptor.

56. The method of claim 33 wherein said polypeptide is contained in a cell.

15

57. The method of claim 33 wherein said molecule is a member selected from antisense DNA, an antisense RNA, a ribozyme, an siRNA, a small organic molecule and an antibody.

20

58. The method of claim 57 wherein said antibody is specific for a polypeptide comprising an amino acid sequence of SEQ ID NO: 806 - 854.

59. A method for identifying an anti-neoplastic agent comprising contacting a cancerous cell with a compound found to have anti-neoplastic activity in the method of claim 59 under conditions promoting the growth of said cell and detecting a change in the activity of said cancerous cell.

25

60. The method of claim 59 wherein said change in activity is a decrease in the rate of replication of said cancerous cell.

30

61. The method of claim 59 wherein said change in activity is the death of said cancerous cell.

62. A method for treating cancer comprising contacting a cancerous  
5 cell with an agent first identified as having gene modulating activity using the method of claim 25, 33, or 59 and in an amount effective to cause a reduction in cancerous activity of said cell.

63. The method of claim 62 wherein said cancerous cell is contacted *in*  
10 *vivo*.

64. The method of claim 62 wherein said reduction in cancerous activity is a decrease in the rate of proliferation of said cancerous cell.

65. The method of claim 62 wherein said reduction in cancerous  
15 activity is the death of said cancerous cell.

66. The method of claim 62 wherein said cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian  
20 cancer, pancreatic cancer, cervical cancer and kidney cancer.

67. A method for treating cancer comprising contacting a cancerous cell with an agent having affinity for an expression product of a gene of Table 1 and in an amount effective to cause a reduction in cancerous activity of said  
25 cell.

68. The method of claim 67 wherein said expression product is a polypeptide.

69. The method of claim 67 wherein said molecule is a member  
30 selected from antisense DNA, an antisense RNA, a ribozyme, an siRNA, a small organic molecule and an antibody.

70. The method of claim 69 wherein said antibody is specific for a polypeptide comprising an amino acid sequence selected from SEQ ID NO: 806 – 854.

5           71. A method for monitoring the progress of cancer therapy in a patient comprising monitoring in a patient undergoing cancer therapy the expression of a gene of Table 1.

72. The method of claim 71 wherein said gene encodes the same gene  
10       product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923.

73. The method of claim 71 wherein said cancer therapy is chemotherapy.

15           74. The method of claim 71 wherein said cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

75. A method for determining the likelihood of success of cancer  
20       therapy in a patient, comprising monitoring in a patient undergoing cancer therapy the expression of a gene of Table 1 wherein a decrease in said expression prior to completion of said cancer therapy is indicative of a likelihood of success of said cancer therapy.

25           76. The method of claim 75 wherein said gene encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923.

77. The method of claim 75 wherein said cancer therapy is chemotherapy.

30

78. The method of claim 744 wherein said cancer is a member selected from breast cancer, colon cancer, lung cancer, prostate cancer, ovarian cancer, pancreatic cancer, cervical cancer and kidney cancer.

79. A method for producing test data with respect to the anti-neoplastic activity of a compound comprising:

(a) identifying a test compound as having anti-neoplastic activity using a method of claim 25;

(b) producing test data with respect to the anti-neoplastic activity of said test compound sufficient to identify the chemical structure of said test compound.

80. A method for producing test data with respect to the anti-neoplastic activity of a compound comprising:

(a) identifying a test compound as having anti-neoplastic activity using a method of claim 33;

(b) producing test data with respect to the anti-neoplastic activity of said test compound sufficient to identify the chemical structure of said test compound.

81. A method for determining the progress of a treatment for cancer in a patient afflicted therewith, following commencement of a cancer treatment on said patient, comprising:

(a) determining in said patient a change in expression of one or more genes of Table 1; and

(b) determining a change in expression of said gene compared to expression of said one or more determined genes prior to said cancer treatment;

wherein said change in expression indicates progress of said treatment thereby determining the progress of said treatment.

82. The method of claim 81 wherein said change in expression is a decrease in expression and said decrease indicates success of said treatment.

- 5           83. The method of claim 81 wherein said gene encodes the same gene product as a polynucleotide of SEQ ID NO: 1 - 805 and 855 - 923.



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ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

(54) Title: DETERMINING CANCER-LINKED GENES AND THERAPEUTIC TARGETS USING MOLECULAR CYTOGE-  
NETIC METHODS

(57) Abstract: Methods for identifying potential therapeutic agents, such as anti-tumor agents, based on their modulation of the expression of specified genes, especially genes mapping to specific chromosomal regions, are disclosed. Also described are methods for diagnosing cancerous, or potentially cancerous, conditions as a result of the expression, or patterns of expression, of such genes, including detecting changes in levels of gene copy number and/or level of amplification of the said gene, or sets of genes, to detect and/or diagnose the cancer. Methods for detecting or determining functionally related genes, as well as methods for treating cancer based on targeting expression products of such genes, determining genes involved in the cancerous process and the success and/or response rates and survival statistics for cancer patients on treatment are encompassed by the invention. Also encompassed are methods involving determining the modulated expression of the genes in these regions of interest (ROIs) as pharmacodynamic/pharmacogenetic/surrogate markers and/or for patient profiling prior to accrual for clinical trials/treatments based on the identification of these genes as validated gene/drug targets in various cancer tissue types.

# INTERNATIONAL SEARCH REPORT

International application No.

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<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC(7) : C12Q 1/68 US CL : 435/6 According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) U.S. : 435/6  Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) Please See Continuation Sheet		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/92581 A2 (CORIXA CORPORATION) 06 December 2001 (06.12.2001), SEQ ID NO:8806, 8674, 8852, 8742, 8737, 8984, and pages 360-448.	1-83
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search 28 December 2004 (28.12.2004)		Date of mailing of the international search report 24 FEB 2005
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230		Authorized officer Kenneth R Horlick Telephone No. 571-272-1600

## INTERNATIONAL SEARCH REPORT

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### Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-83 (partial) regarding SEQ ID NO:1

Remark on Protest

☐  
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US04/09289

### BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1, claim(s) 1-83 (partial), drawn to methods of diagnosing cancer relating to SEQ ID NO:1.

Groups 2-874, claim(s) 1-83 (partial), drawn to methods of diagnosing cancer relating to SEQ ID NO:2-805 and 855-923, respectively.

The inventions listed as Groups 1-874 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: each of the groups relates to a nucleic acid having a structure which is not shared with any of the other nucleic acids; thus, the special technical feature of each Group is the structure of the nucleic acid, defined by its nucleotide sequence. So there is no common structure among the nucleic acids of the different Groups.

Continuation of B. FIELDS SEARCHED Item 3:  
USPAT, PGPUB, DERWENT WPI, MEDLINE, BIOSIS, GENEMBL, GENESEQ  
search terms: cDNA, gene, cancer, SEQ ID NO:1